Évaluation de l'efficacite et de la morphologie de la sclerectomie profonde avec implant collagène dans l'espace suprachoroïdien

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Département de Neurosciences Clinique
Service d'Ophtalmologie

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"Évaluation de l'efficacite et de la morphologie de la sclerectomie profonde avec implant collagène dans l'espace suprachoroïdien"

Thèse
Présentée à la Faculté de Médicine
De l'Université de Genève
Pour obtenir le grade de Doctorat en Médicine
Par

Rany MITWALLY

Du

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Rany MITWALLY

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Evaluation de l'efficacité et de la morphologie de la sclérectomie profonde avec implant collagène dans l'espace suprachoroïdieen

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Genève, le 19 septembre 2017

Thèse n° **10858**

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N.B. - La thèse doit porter la déclaration précédente et remplir les conditions énumérées dans les "Informations relatives à la présentation des thèses de doctorat à l'Université de Genève".

Résumé

La sclérectomie profonde (SP) avec implantation d'un dispositif de maintien dans I'espace suprachoroïdien (SPICS) est une technique chirurgicale d'intervention de filtration pour le traitement du glaucome qui est relativement nouvelle. La présente thèse est sur une étude controlée prospective, non-randomisée et multicentrique pour l'évaluation de la SPICS. Les principaux objectifs de cette étude sont d'étudier l'efficacité de la SPICS, d'évaluer la morphologie des bulles de filtration par I'UBM, et enfin d'évaluer le rôle du flux suprachoroïdien dans la SP.

Le taux de succès complet à 12 mois était de 86% et la réduction de pression intra-oculaire (PIO) était de 5l.4%. La présence simultanée d'un espace intra-scléral, d'une bulle sous-conjonctivale et d'une zone hypoéchogène supra ciliaire, a été associée à l'abaissement de la PIO et au taux de réussite. Le débit suprachoroïdien semble jouer un rôle dans la réduction de la PIO. L'effet à long terme doit encore être évalué.

CONTENTS:

ABBREVIATIONS:

AC:	Anterior Chamber
DS:	Deep Sclerectomy
DSCI:	Deep Sclerectomy with Collagen Implant
DS-MMC:	Deep Sclerectomy with Mitomycin C
DSSCI:	Deep Sclerectomy with Suprachoroidal Collagen Implant
IOP:	Intraocular Pressure
MMC:	Mitomycin C
NGPS:	Non-Penetrating Glaucoma Surgery
OAG:	Open Angle Glaucoma
PI:	Peripheral Iridectomy
PAS:	Peripheral Anterior Synechia
POAG:	Primary Open Angle Glaucoma
SC:	Schlemm's Canal
TDM:	Trabeculo-Descemetic Membrane
UBM:	Ultrasound Biomicroscopy
VC:	Viscocanalostomy

1. INTRODUCTION:

The definitions of glaucoma have evolved over the past century[1], and until this day remain inexact and subject to adjustment. Currently the term refers to a group of diseases, rather than a single entity, that differs in their pathophysiology, clinical presentation, and management. Glaucoma is a group of diseases affecting the optic disc in the form of pathological characteristic excavation. The hallmark of this optic neuropathy is defects in the nerve fiber layer associated with corresponding visual field defects. Glaucoma is often, but not always, associated with elevated levels of intraocular pressure (IOP).[2]

The treatment of glaucoma is by three routes; medical treatment, laser therapy and/or surgical intervention. Trabeculectomy has always been considered the most effective and reproducible surgical method for reducing IOP levels.[3] It's capability in lowering IOP to levels that are sufficient to protect the optic nerve head and retinal never fiber layer from further damage has made it the yardstick to which all other filtering surgeries are compared.[4] However, its complications are numerous; including hypotony, cataract formation and progression; choroidal effusion, hyphema, bleb scaring, and bleb-related endophthalmitis.[5]

Non-penetrating glaucoma surgery (NPGS) has been established as an alternative method to trabeculectomy due its similar effectiveness in reducing IOP, but with less postoperative complications. Although numerous NPGS techniques have been described, NPGS generally refers to deep sclerectomy (DS), viscocanalostomy (VC) and canaloplasty.[6]

Deep sclerectomy is a filtering procedure that allows flow of aqueous humor from the anterior chamber to the subconjunctival space through the trabeculo-descemetic membrane (TDM), a naturally occurring membrane. The TDM prevents postoperative hypotony by functioning as an outflow resistance site.[6] Other advantages of DS are the minimal changes in the refractive state of the cornea,[7] low incidence of postoperative anterior chamber (AC) inflammation,[8] and the inferior rate of cataract formation in comparison to trabeculectomy.[9] Although DS results have been satisfactory in primary and secondary open angle glaucoma (OAG), it's efficacy remains dubious in the presence of a closed or neovascularised angle.[10]

In DS, a scleral flap similar to a trabeculectomy flap is first created. Deeper to the superficial flap the surgeon dissects and excises a deeper portion of sclera, revealing the surgically created TDM. Aqueous humor, after passing through the TDM, may be eliminated through four possible routes; by the way of a filtering bleb in the subconjunctival space, via the intrascleral space (also termed the intrascleral cavity, decompression space or the scleral lake), by suprachoroidal (supraciliary) filtration and by drainage into the episcleral veins through canal of Schlemm.[11]

Secondary fibrosis of the intrascleral filtering bleb is a common problem in DS, and may lead to failure of IOP regulation. To augment the filtering effects of deep sclerectomy, Koslov et al[12] proposed the placement of an implant made of collagen in the intrascleral cavity. The concept of this collagen device was to fill the intrascleral space beneath the superficial flap during the early postoperative period when the process of healing is at its maximum. The collagen implant is later resorbed, leaving an empty cavity to which aqueous is drained and then absorbed; therefore acting as a space maintaining device. These space maintaining devices can be also placed beneath the intrascleral space into the underlying suprachoroidal space.[13]

In the 1960's, Anders Bill reported the presence of an unconventional route of aqueous outflow, the uveoscleral pathway.[14,15] He suggested that this route accounts for approximately 20% of aqueous humor elimination, and by using this route, enhancement of IOP reduction may occur. However, the concept of lowering IOP by shifting aqueous into the suprachoroidal space is not a novel technique. At the end of the 19th century, Ernst Fuchs discovered the presence of a cyclodialysis cleft, a space between the scleral spur and root of the iris that would accidentally and infrequently open up during cataract surgery.[16] Due to a pressure gradient between the anterior chamber and suprachoroidal space, aqueous humor drained with limited control through this gap, resulting occasionally in extremely low pressures. In 1905, Leopold Heine established a method to utilize the cyclodialysis cleft by producing an instrument, the cyclodialysis spatula.[17] The main disadvantage of this approach was that in the absence of a mechanism to maintain this space, the cleft was prone to sudden closure, resulting in painful and severe IOP spikes. This technique was largely deserted until 1967 when James Gills proposed the insertion of an implant made of Teflon.[18] This procedure experienced an initial degree of success, but the size and material of the Teflon implant resulted in poor long-term outcomes. The utilization of the suprachoroidal route to improve aqueous humor elimination and therefore reduction of IOP, (through both medical and surgical means) is one of the current challenges in the management of glaucoma.[13]

Anterior segment imaging, as ultrasound biomicroscopy (UBM), allows precise measurements of the anterior segment.[19,20] It permits the visualization and assessment of structures that cannot be visualized by routine slit lamp examination. Recently, UBM has been used to analyze bleb morphology after glaucoma surgery.[21]

2. OBJECTIVE OF STUDY:

The study is divided into **two** parts: (i) a prospective, non-randomized, controlled, multicenter evaluation of the safety and efficacy of deep sclerectomy with suprachoroidal collagen implant (DSSCI) (ii) prospective, non-randomized, single center controlled study to evaluate bleb morphology of DSSCI after one year.

The primary objectives of this study are the following:

1) To evaluate the safety and efficacy of this procedure.
2) To study the morphology of the filtering blebs after one year by UBM imaging.
3) To analyze if insertion of the collagen implant into the suprachoroidal space leads to formation of a patent bleb in that region.
4) To assess the role of suprachoroidal outflow in DS.

3. AQUEOUS HUMOR OUTFLOW:

Aqueous humor is produced by the non-pigmented epithelium of the ciliary processes in the posterior chamber of the eye. Aqueous is then eliminated through two routes; the conventional and unconventional pathways. The conventional pathway consists of trabecular meshwork (uveal, corneoscleral & juxtacanalicular), Schlemm's canal (SC), collector channels, intrascleral venous plexus, aqueous veins, episcleral veins and conjunctival veins. This pathway accounts for 43-75% of aqueous outflow[22] **(Figure 3.1)**. The unconventional pathway, which is through the uveoscleral complex, drains around 25-57% of the aqueous-humor production.[22]

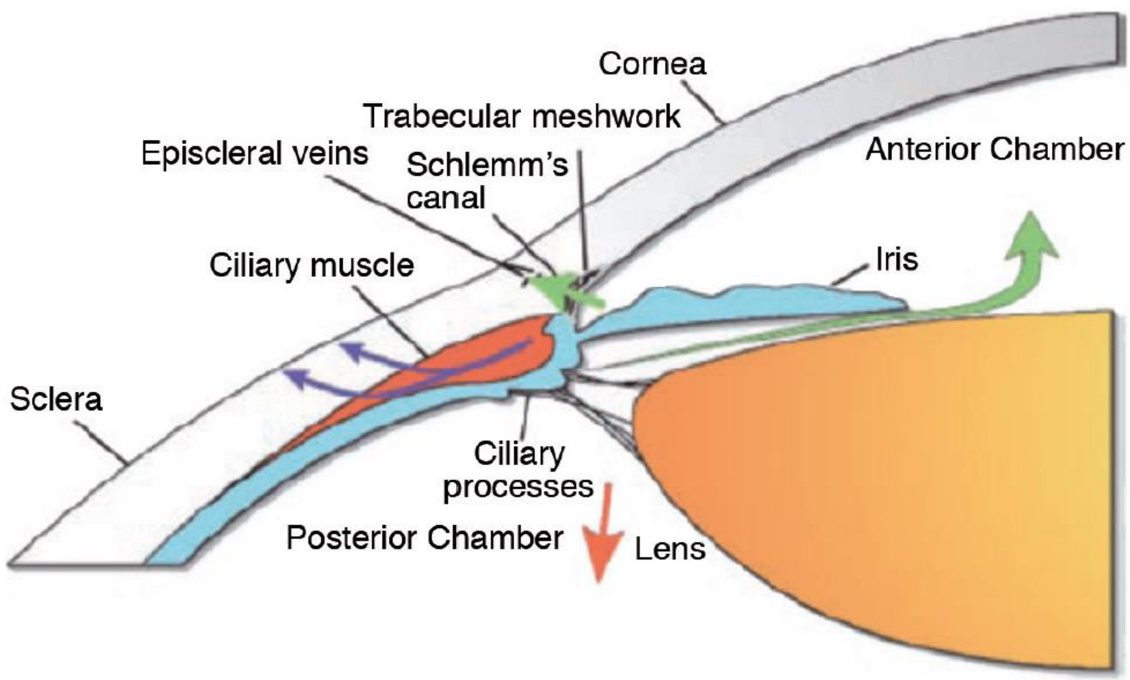

Figure 3.1: Circulation and drainage of aqueous humor. *Choplin E Lundy D. Atlas of Glaucoma, Second Edition. Ed Informa, 2007 UK.*

A. TRABECULAR MESHWORK:

The trabecular meshwork is made up of connective tissue strands arranged as superimposed perforated sheets, comprising three layers **(Figure 3.2)**. The inner layer is the uveal meshwork, which is an extension of the ciliary muscle. The middle layer, the corneoscleral meshwork, is located between the line of Schwalbe and scleral spur.[23] The outer layer is the juxtacanalicular meshwork (which is situated between the corneoscleral meshwork and the canal of Schlemm's inner wall) which is a rich cell-zone consisting of 2-5 layers of cells, situated within an extracellular matrix.[23] The spaces of the trabecular meshwork, through which aqueous humour can percolate, decrease in size progressively from within outwards.

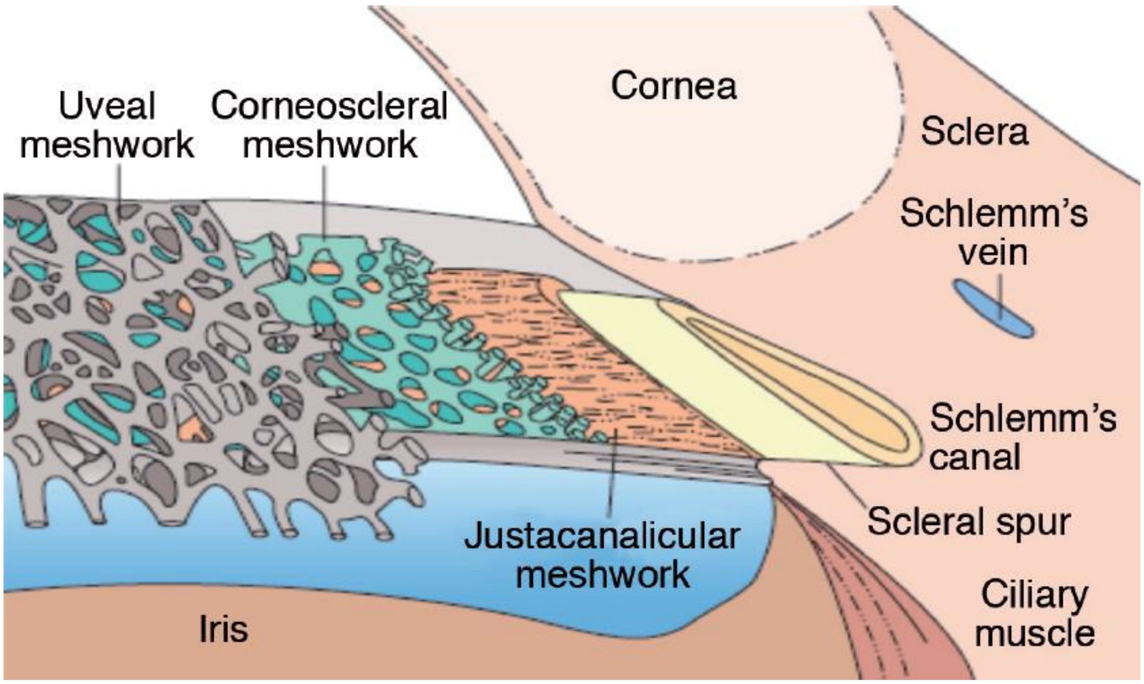

Figure 3.2 : Anatomy of the trabecular meshwork. *Choplin E Lundy D. Atlas of Glaucoma, Second Edition. Ed Informa, 2007 UK.*

B. CANAL OF SCHLEMM AND COLLECTOR CHANNELS:

The canal of Schlemm is a circular tube which communicates around the entire eye globe and measures 36 mm in circumference (**Figure 3.3**). The canal lumen is lined by endothelium similar to vascular endothelium.[23] The diameter of the lumen may differ according to the level of IOP, becoming very narrow at high pressures or wide at low pressures.[24]

The collector channels, which arise from the canal of Schlemm, are 25-35 in number and drain into three interconnecting venous plexuses.[25] A small number of these channels (4-6) drain directly into the episcleral venous plexus and are known as aqueous veins. Through these collector channels, aqueous humor flows from the trabecular meshwork to the episcleral venous network.[26]

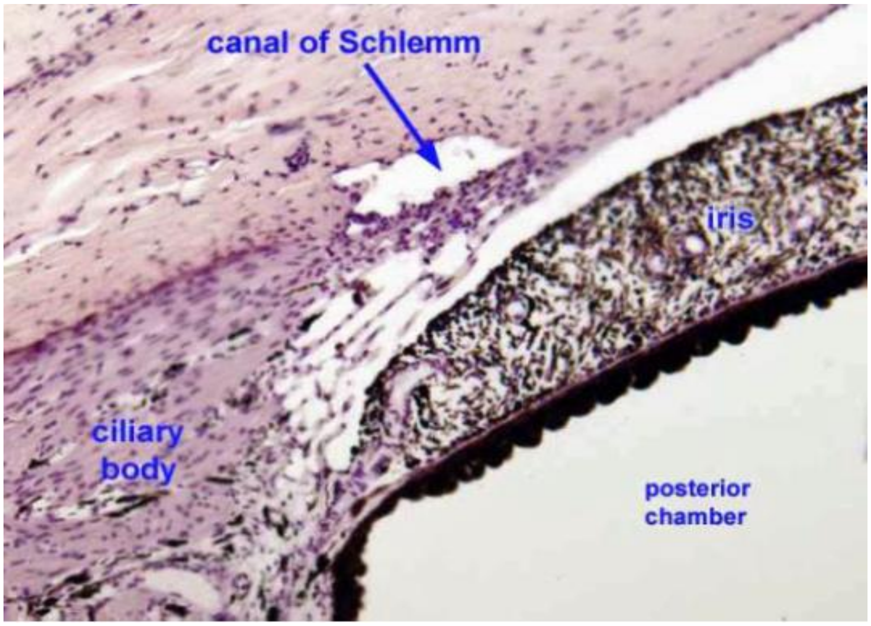

Figure 3.3: Canal of Schlemm. *Ethier CR. The inner wall of Schlemm's canal. Exp Eye Res.2002; 74:161-172.*

C. UVEOSCLERAL FLOW:

Uveoscleral outflow (the unconventional pathway) is the drainage of aqueous humor through the ciliary muscle, the iris, sclera and other neighboring structures **(Figure 3.4)**. Uveoscleral outflow is reported to be up to 35 % of total flow, and can increase up to almost four-folds with anterior segment inflammation.[27] Aqueous humor leaves the AC and enters the ciliary body and hence into the supraciliary and suprachoroidal compartments. This fluid then exits the suprachoroidal space either by absorption into the uveal vascular system or by diffusion through the sclera.[28]

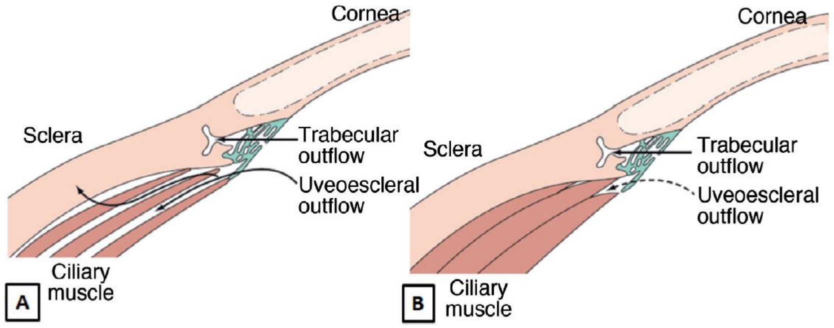

Figure 3.4: Ciliary muscle and its behavior with respect to uveoscleral flow. A) Relaxed Muscle: The aqueous humor flows easily between the muscle fibers. B) Longitudinal Muscle Contracted: Circulation through the fibers is impaired. *Choplin E. Lundy D. Atlas of Glaucoma, Second edition. Ed Informa, 2007 UK.*

4. SURGICAL ANATOMY:

A. LIMBUS:

The limbus consists of a surgical and anatomical part. The surgical limbus, which is the site of glaucoma filtration surgery, is a broad area of transition between clear peripheral cornea and opaque sclera marked by a prominent ridge created by insertion of conjunctiva and Tenon's capsule into the cornea (**Figure 4.1**) It has a bluish-grey appearance, with a width of approximately 1.2 mm. The anatomical limbus is a circumcorneal transitional zone between the conjunctivocorneal and sclerocorneal junction. The limbus is wider superior, making the cornea horizontally oval. Internally, Schwalbe's line is a ring with an almost perfectly circular appearance.[29]

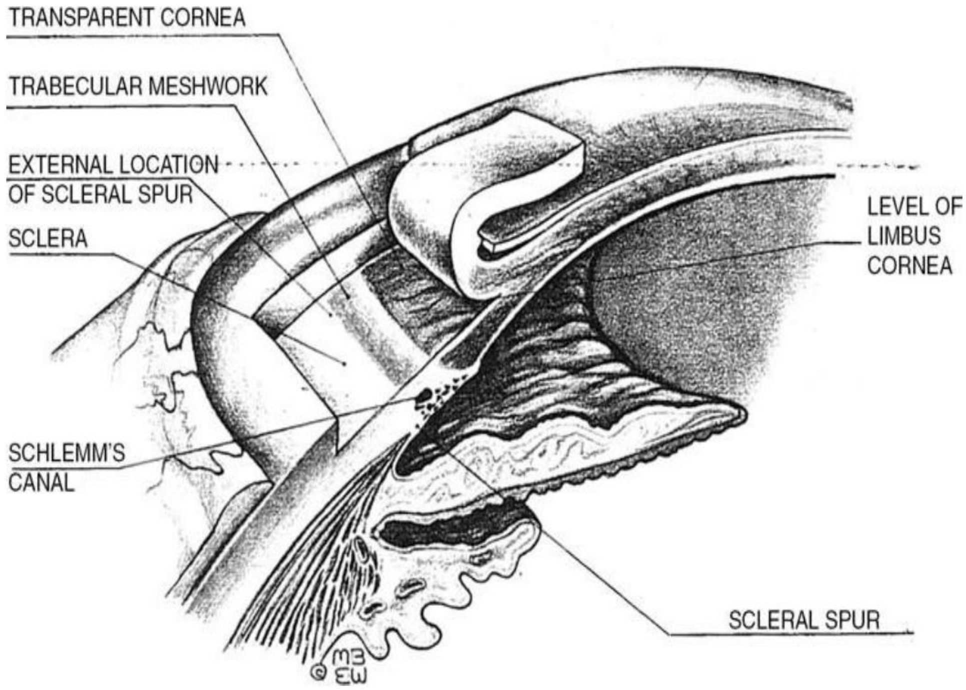

Figure 4.1: Diagram of the angle structures after creation of superficial sclera flap. *Maurice H, Graham E: Glaucoma Surgeries, Glaucoma Surgical Anatomy, 2005. Courtesy of Taylor & Francis Group, permission granted for use*

B. INCISIONS:

Incision at the site of the conjunctival insertion directed towards the anterior chamber will run immediately into clear corneal tissue, piercing the chamber wall anterior to the line of Schwalbe.[30]

In most wide-angled eyes, entry into the anterior chamber at the mid-trabecular region can be achieved when the incision is made at at the corneoscleral sulcus, exactly perpendicular to the surface of the globe. However, in eyes with a narrow anterior chamber angle, incision through this point may result in entry into the angle recess or even the ciliary body.[30]

An important and distinct landmark is the color change from the white of the sclera to the bluish hue derived from the cornea merging with the sclera. At this junction, the scleral spur is situated; and just anterior to it is the canal of Schlemm.[31]

C. CANAL OF SCHLEMM:

This structure can be located approximately 2.0 mm posterior to the surgical limbus.[30]

D. SUPRACHOROIDAL (SUPRACILIARY) SPACE:

The suprachoroidal or supraciliary space is a potential space between the choroidal and ciliary portions of the uveal tract, and the sclera. In this plane, the uvea and sclera are loosely attached.[32] To reach the suprachoroidal space, an incision is made in the deep scleral bed, 1–1.5 mm posterior to the canal of Schlemm.[13]

5. REVIEW OF NON-PENETRATING GLAUCOMA SURGERIES:

A. HISTORICAL REVIEW:

The first report on sinusotomy was published by Krasnov[33] which involved removal of a portion of the sclera and deroofing the canal of Schlemm over 140 degrees superiorly without creating a scleral flap. The Schlemm‘s canal inner wall was left intact. In non-penetrating trabeculectomy, a thin scleral flap is created and the excision of the juxtacanalicular trabecular meshwork with inner wall of Schlemm's canal is performed at the dissected site. This procedure was described by Zimmermann.[34] Fyodorov reported removing the stroma of the cornea posterior the trabeculum and the DM; and the operation was termed ‘deep sclerectomy’.[35] This procedure was also described by Kozlov[12], and sometime after by Stegmann[30] as ‘viscocanalostomy’ where viscoelastic material was injected into the two cut ends of SC.

B. TYPES OF NPGS:

1. DEEP SCLERECTOMY (DS):

A superficial sclera flap, around 30% of the scleral thickness, is created with dimensions of roughly 5 × 5 mm using a number 11 blade.[36] In order to expose the trabeculo-descemetic membrane (TDM), dissection of the superficial sclera flap should be advanced 1-1.5 mm into the cornea anteriorly. In refractory cases, a sponge soaked in mitomycin C (MMC) 0.28 mg/ml can be applied for 1-3 minutes on the sclera surface and under the conjunctiva, before or after dissection of the superficial flap.[36]

Deep scleral dissection (hence the name ‘deep sclerectomy’) is achieved using a crescent knife by making a deeper flap 4 × 4 mm within the bed of the previously dissected flap, therefore by definition becoming smaller in size compared to the superficial flap[37] **(Figure 5.1).**

The initial incision should be sufficiently deep until choroid is exposed.[37] With the use of a crescent knife, dissection continues anteriorly, making sure that bisection of the canal of Schlemm‘s canal is performed. The Schlemm’s canal is located anterior to the scleral spur, just as the fibers of the sclera start to have a regular parallel pattern in relation to the limbus **(Figure 5.2)**.

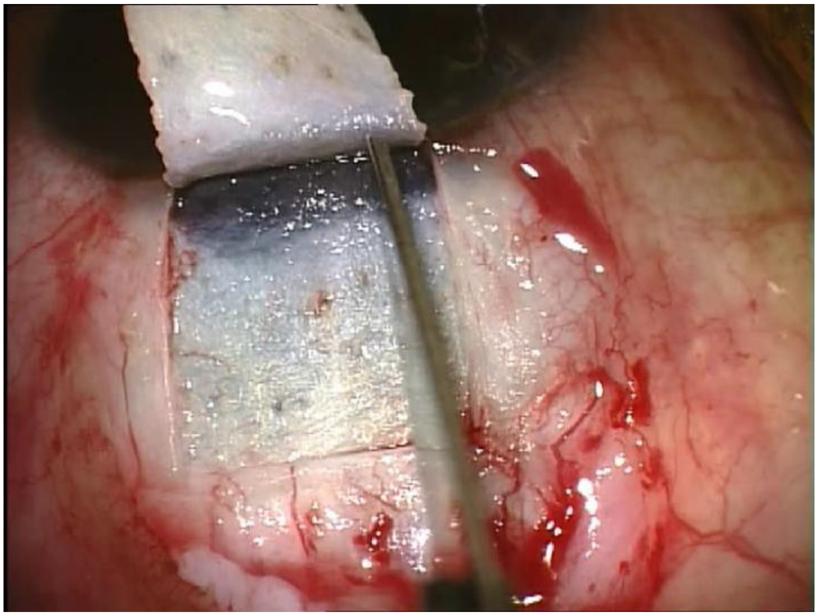

Figure 5.1: Creation of the superficial scleral flap is done by dissecting around 30% of the scleral thickness with advancement of 1-1.5mm into the cornea. *Private collection of Tarek Shaarawy (TS), permission granted for use*

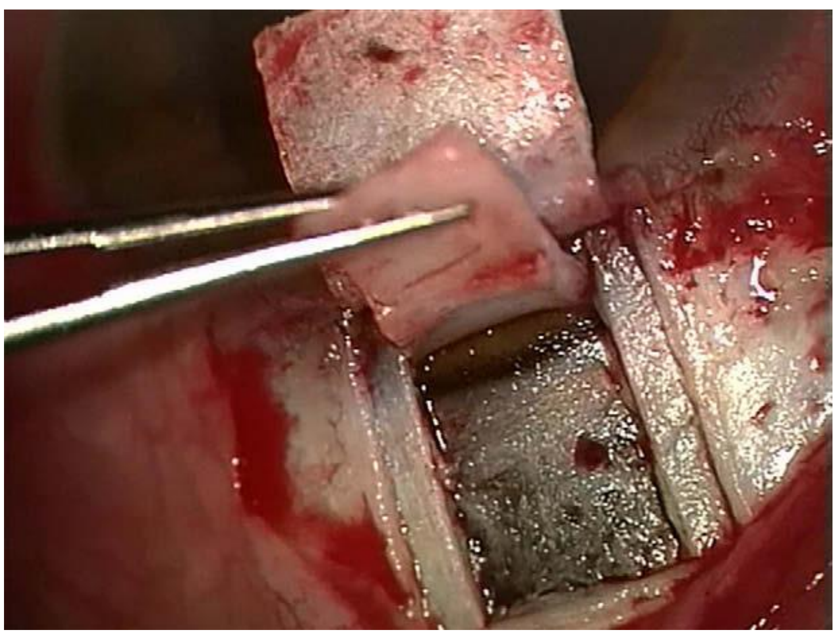

Figure 5.2: Creation of the deep scleral flap. *Private collection of André Mermoud (AM), permission granted for use*

The dissection is carried on anteriorly after deroofing the Schlemm's canal has been done. This step is essential in order to create a large TDM which will allow for Nd:YAG goniopuncture (if needed later on) and decreasing the risk of iris incarceration if the goniopuncture is made near the iris. To avoid perforation during this step, the corneal stroma and Descemet's membrane (DM) are gently separated by applying pressure on the scleral bed near the end of the dissection using a blunt instrument as a sponge. The dissection is extended anteriorly by performing radial cuts using a No. 11 blade, with special care given to avoid contact with the TDM[37] **(Figure 5.3)**.

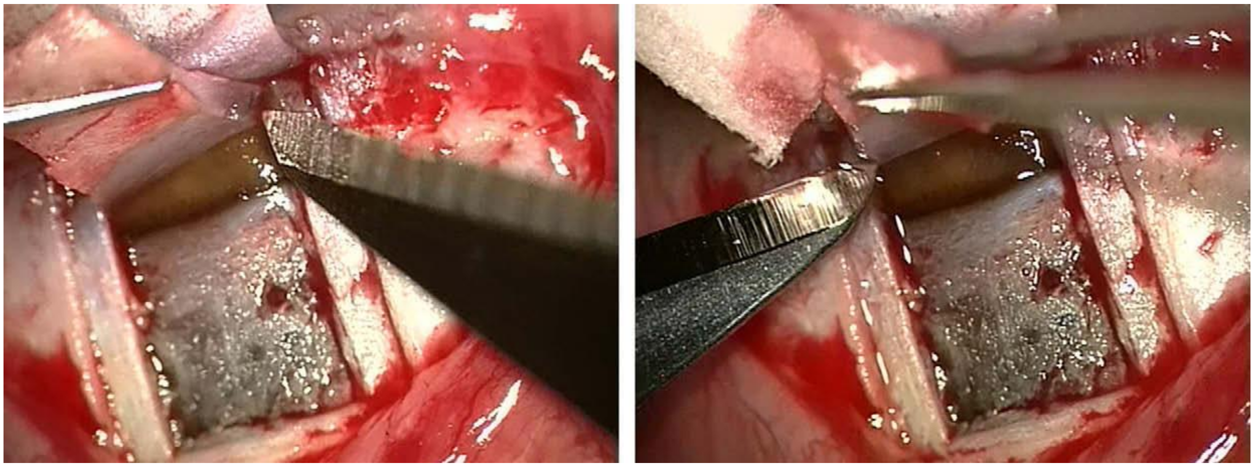

Figure 5.3: Further lateral dissection with a No.11 blade on both sides into clear cornea and which better exposes the trabeculo-Descemet's membrane. *Mendrinos E, Mermoud A, and Shaarawy T: Nonpenetrating Glaucoma Surgery, Diagnostic and Surgical Technique. Survey of Ophthalmology, Nov-Dec 2008. Courtesy of Elsevier, permission granted for use*

Excision of the deep scleral flap is then carried out using blunt scissors **(Figure 5.4)**. Using small blunt forceps, the inner wall of Schlemm's canal and the adjacent trabeculum (which appear as a thin elastic membrane just anterior to the scleral spur) are peeled off **(Figure 5.5)**. Removal of these structures is called ab-externo trabeculectomy.[38] In order to preserve the patency of the cavity created in the sclera, insertion of a space occupying implant can be done **(Figure 5.6)**.

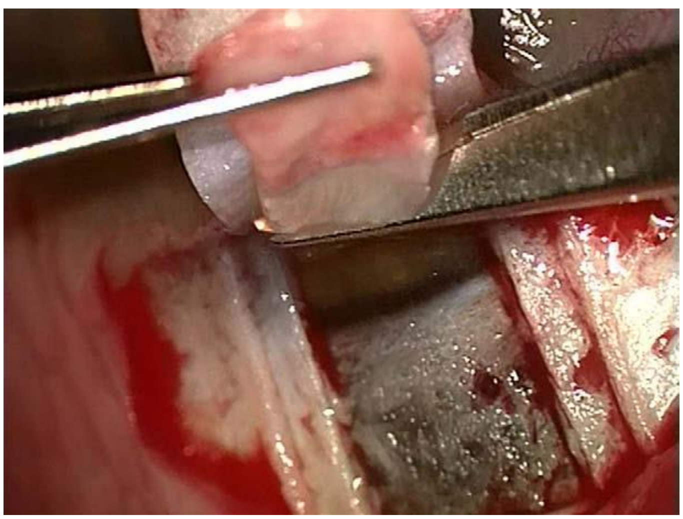

Figure 5.4: Using a Gallan scissor, the deep scleral flap is removed. At that stage of the procedure, there should be an evident percolation of aqueous humor through the trabeculo-Descemet's membrane. *Mendrinos E, Mermoud A, and Shaarawy T: Nonpenetrating Glaucoma Surgery, Diagnostic and Surgical Technique. Survey of Ophthalmology, Nov-Dec 2008. Courtesy of Elsevier, permission granted for use*

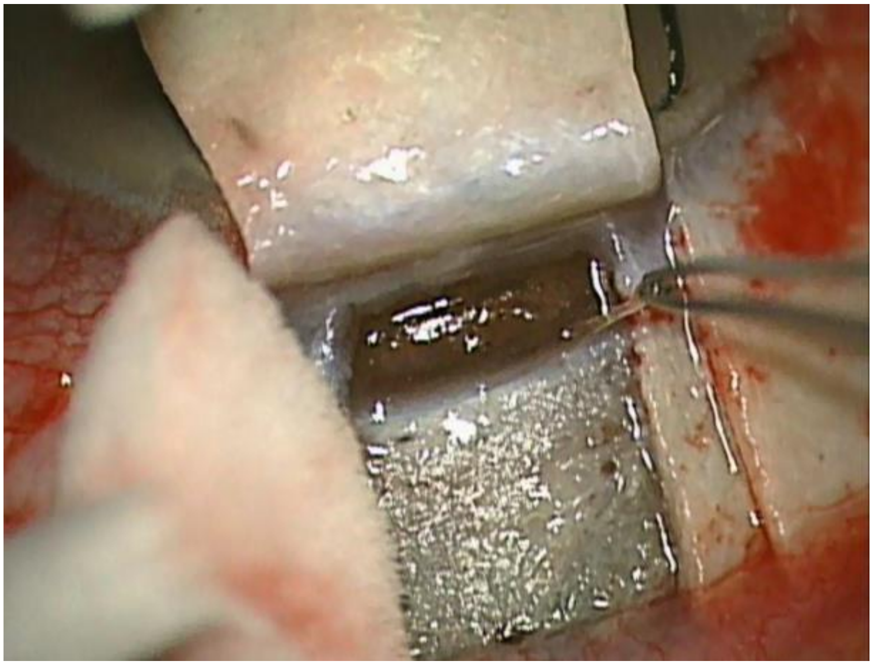

Figure 5.5: The inner wall of the Schlemm's canal and the juxtacanalicular trabeculum are peeled off using fine forceps. *Mendrinos E, Mermoud A, and Shaarawy T: Nonpenetrating Glaucoma Surgery, Diagnostic and Surgical Technique. Survey of Ophthalmology, Nov-Dec 2008. Courtesy of Elsevier, permission granted for use*

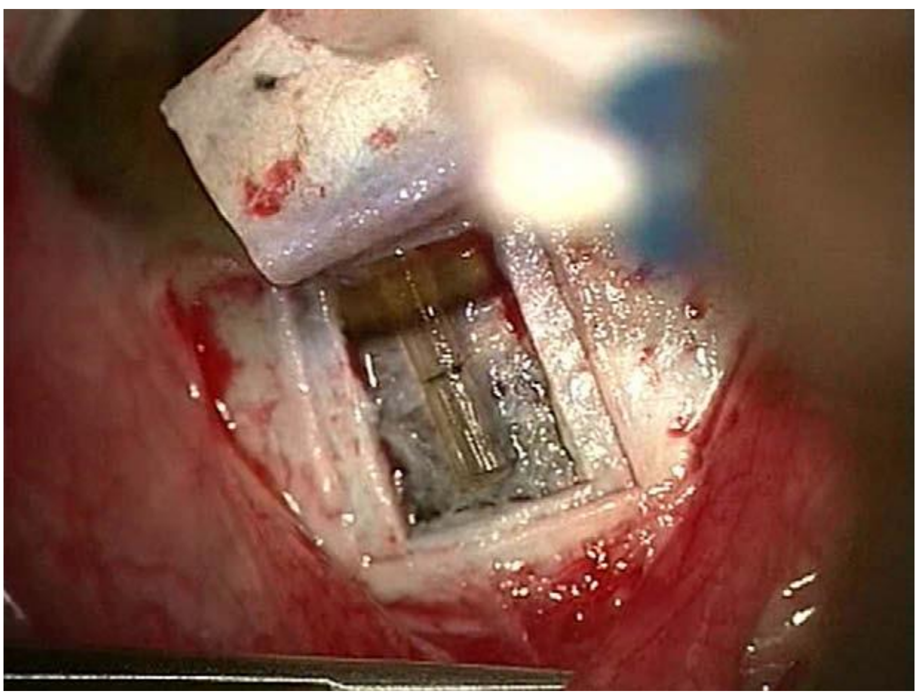

Figure 5.6: A collagen implant is sutured in the scleral bed. This implant will serve as a space maintainer to create an intrascleral space for aqueous humor to filter. *Mendrinos E, Mermoud A, and Shaarawy T: Nonpenetrating Glaucoma Surgery, Diagnostic and Surgical Technique. Survey of Ophthalmology, Nov-Dec 2008. Courtesy of Elsevier, permission granted for use*

The Use of Implants in Deep Sclerectomy:

Secondary fibrosis of the filtering blebs in DS is an important obstacle towards obtaining long term success and subsequent control of IOP. To tackle this issue, Koslov et al[12] reported the use of a collagen device inserted within the scleral bed. The concept of the collagen implant was to fill the intrascleral space under the superficial flap during the early postoperative period where the healing process is at its maximum. The collagen implant is later resorbed, leaving an empty cavity to which aqueous is filtered to and then absorbed.[38]

Other implants, of the same function and different design, have been also proposed;[39-46] and just recently, implants have been placed beneath the scleral bed into the underlying suprachoroidal space.[13] **(Figures 5.7 & 5.8)**.

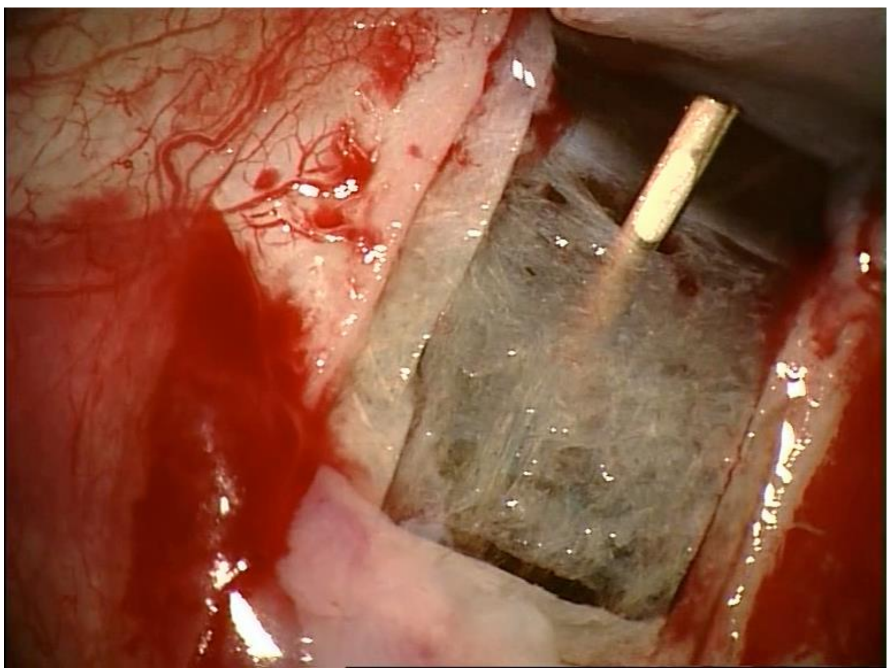

Figure 5.7: Collagen implant in the suprachoroidal space under the remaining thin layer of sclera. *Private collection of TS, permission granted for use*

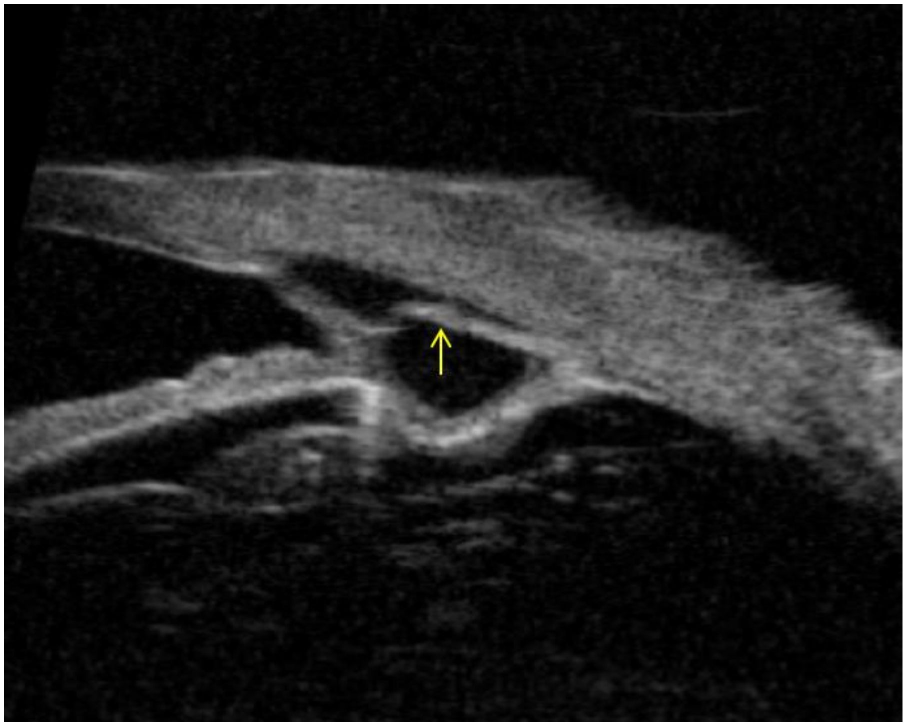

Figure 5.8: UBM showing the collagen implant in the suprachoroidal space (arrow); creating a suprachoroidal filtering bleb with the thin remaining scleral layer above, the choroid below and the TDM membrane in front. *Private collection of TS, permission granted for use*

Types of Implants:

1) ***Collagen Aquaflow® Implant (STAAR Surgical AG, Switzerland)*:** is a dehydrated purified collagen of porcine origin material. The implant has a cylindrical form (4 × 1 × 1mm).[45-47] **(Figure 5.9)**. Once exposed to the aqueous humor, this implant will significantly swell occupying the intrascleral pace and preventing fibrosis. The implant is resorbed 6 to 9 months later.[39]

Figure 5.9: Collagen Aquaflow implant. *Private collection of AM, permission granted for use*

2) ***Hyaluronic Acid Gel*: *(HealaFlow®, Anteis, Switzerland; NASHA; Q-Med AB, Uppsala, Sweden)*:** is made of reticulated hyaluronic acid, and is injected under the superficial scleral flap into the intrascleral cavity to act as a space maintainer[11,49]. In unpublished study carried

out at Clinique de Montchoisi, Lausanne, Switzerland; HealaFlow was injected into the suprachoroidal space by creating a window in the remaining deep scleral bed (by removing a square portion of the scleral tissue) **(Figure 5.10).**

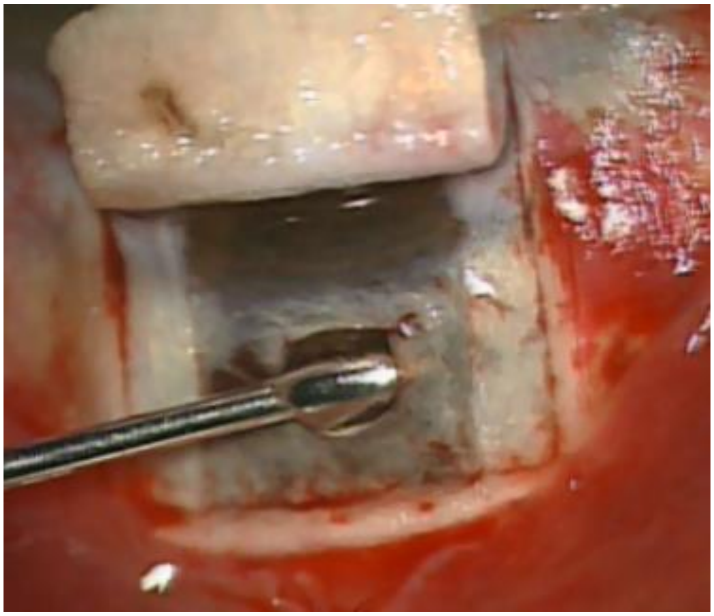

Figure 5.10: RHAI injected into the suprachoroidal space through the created window in the deep scleral bed. *Private collection of AM, permission granted for use*

3) ***T-Flux Implant (IOLTECH Laboratories, La Rochelle, France)***: is T-shaped, non-absorbable, hydrophilic implant[48] **(Figure 5.11)**. Each arm of the T is placed into one of the surgically created ostium's of the canal of Schlemm, and the implant can be secured with a 10-0 nylon suture into a hole present in its foot. The T-Flux implant can be placed in the scleral bed or into the suprachoroidal space.[13]

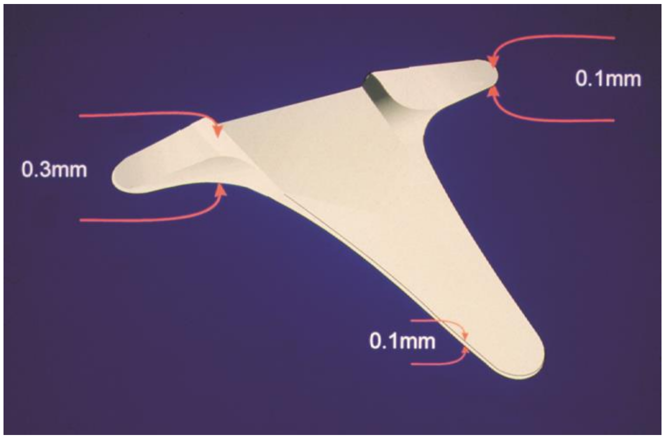

Figure 5.11: T-Flux implant. *Private collection of AM, permission granted for use*

4) ***Esnoper V-2000 Implant*:** is Spanish-made; non-absorbable and trapezoidal in shape, and can be placed in the intrascleral cavity or suprachoroidal space **(Figure 5.12)**. It prolongs the aqueous humor drainage in NPGS in open angle glaucoma. It has a size of 2.85 × 3 × 1.4 mm, and 0.3 mm in thickness. It has 2 holes, one for fixation to the sclera, and the other to improve the aqueous humour filtration; and longitudinal channels to maximize the effect of aqueous humor flow.[39] A new Esnoper implant, called the Esnoper Clip®, has been recently developed; and can be placed in both suprachoroidal and intrascleral space **(Figure 5.13)**.

5) ***Reticulated Hyaluronic Acid Implant (SK-GEL, Corneal, Paris, France)*:** is a gelatinous implant, made of sodium hyaluronate, and can be molded into the desired shape[50] **(Figure 5.14)**. The absorption time in humans has not been figured out yet; but an experimental study showed that it was absorbed at approximately 2 months in rabbits. [11]

6) ***Polymethylmethacrylate (PMMA) Implant:*** Mansouri et al[41] studied on rabbit eyes, the features of a PMMA implant in comparison with the typical cylindrical collagen implant for DS. The device was X-shaped; measuring 4 x 4 mm **(Figure 5.15)**. The implant displayed encouraging results, showing similar characteristics to collagen implants.[41]

Figure 5.12: Esnoper® V-2000 implant. *Courtesy of AJL, S.A.*

Figure 5.13: Esnoper Clip®. *Courtesy of AJL, S.A.*

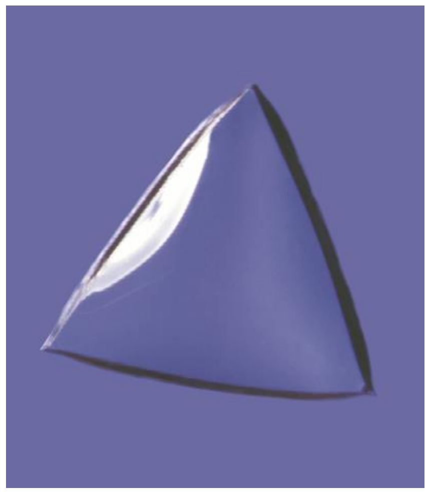

Figure 5.14: SK-GEL implant, cut into a triangular shape. *Private collection of AM, permission granted for use*

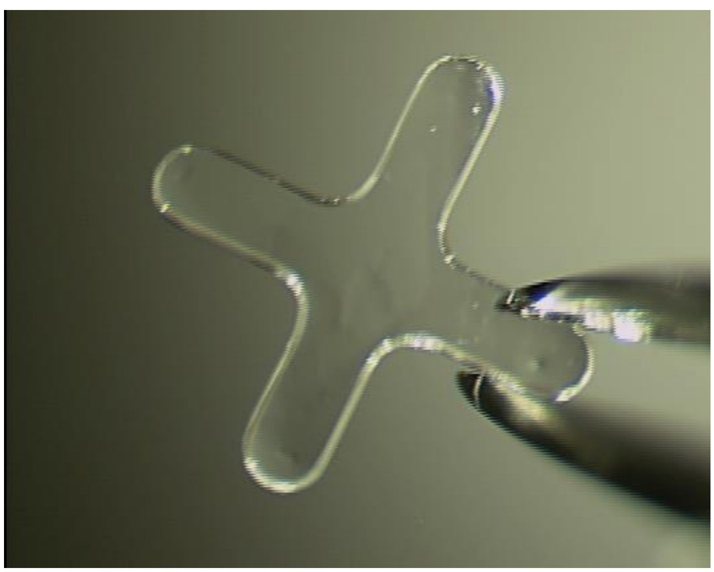

Figure 5.15: PMMA X-shaped implant. *Private collection of AM, permission granted for use*

2. VISCOCANALOSTOMY (VC):

Viscocanalostomy is non-penetrating surgical procedure involving the entire circumference of Schlemm's canal without creating a bleb or performing a fistula. This operation was first described by Stegmann et al.[30] Triangular or square-shaped superficial and deep scleral flaps are fashioned (similar to deep sclerectomy), creating ostia in the canal of Schlemm. Sodium hyaluronate of high-viscosity is injected into Schlemm‘s canal to improve aqueous drainage by this route[30] **(Figure 5.16)**.

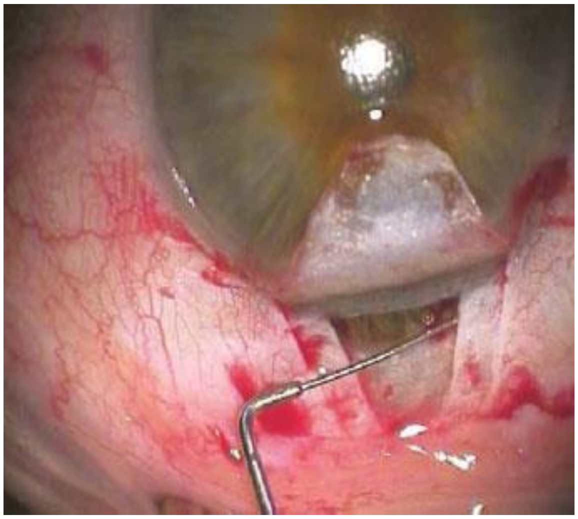

Figure 5.16: Injection of Healon GV into the ostia of Schlemm’s canal with a special cannula. *Scharioth GB: Canaloplasty Re-establish the Natural Outflow in Patients with Chronic Open-Angle Glaucoma. Journal of Current Glaucoma Practice, Jaypee Journals 2009*

3. CANALOPLASTY:

Canaloplasty is a modification of viscocanalostomy, utilizing a microcatheter or tube to dilate the canal of Schlemm. The catheter is slowly placed into the canal, cannulating its whole circumference. Viscoelastic material is injected into the canal of Schlemm. A 10/0 suture is then attached to the ends of the microcatheter and as the catheter is withdrawn, with the suture being left inside the lumen of the canal.[51] **(Figure 5.17).**

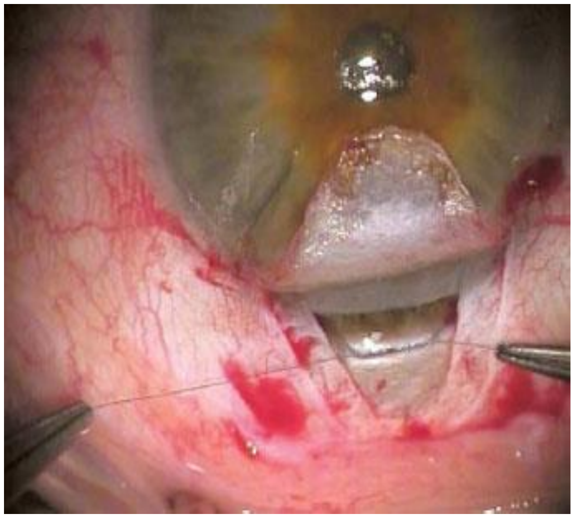

Figure 5.17: Canaloplasty; tying of the suture which has been placed in the lumen of the canal of Schlemm. *Scharioth GB: Canaloplasty Re-establish the Natural Outflow in Patients with Chronic Open-Angle Glaucoma. Journal of Current Glaucoma Practice, Jaypee Journals 2009*

4. CO_2 LASER-ASSISTED SCLERECTOMY SURGERY (CLASS):

In NPGS, the dissection of the deep scleral flap is the most troublesome part, requiring experience and precision. When performing manual dissection with a blade, unintentional perforation of the thin TDM is a common adverse event that takes place in nearly 30% of the patients in the beginning of the learning phase, and in 3% in the hands of experienced surgeons.[52]

CO_2 laser irradiation, because of its unique characteristics, was suggested by Assia et al[53,54] as a way of making deep sclerectomy less difficult. After the superficial flap is fashioned, repeated applications of CO_2 laser leads to progressive ablation of the deep scleral tissue until percolation of aqueous is accomplished **(Figure 5.18)**. The percolating fluid absorbs the laser energy, and ablation automatically stops, disallowing further ablation, and avoiding penetration of the remaining thin scleral tissue.[55]

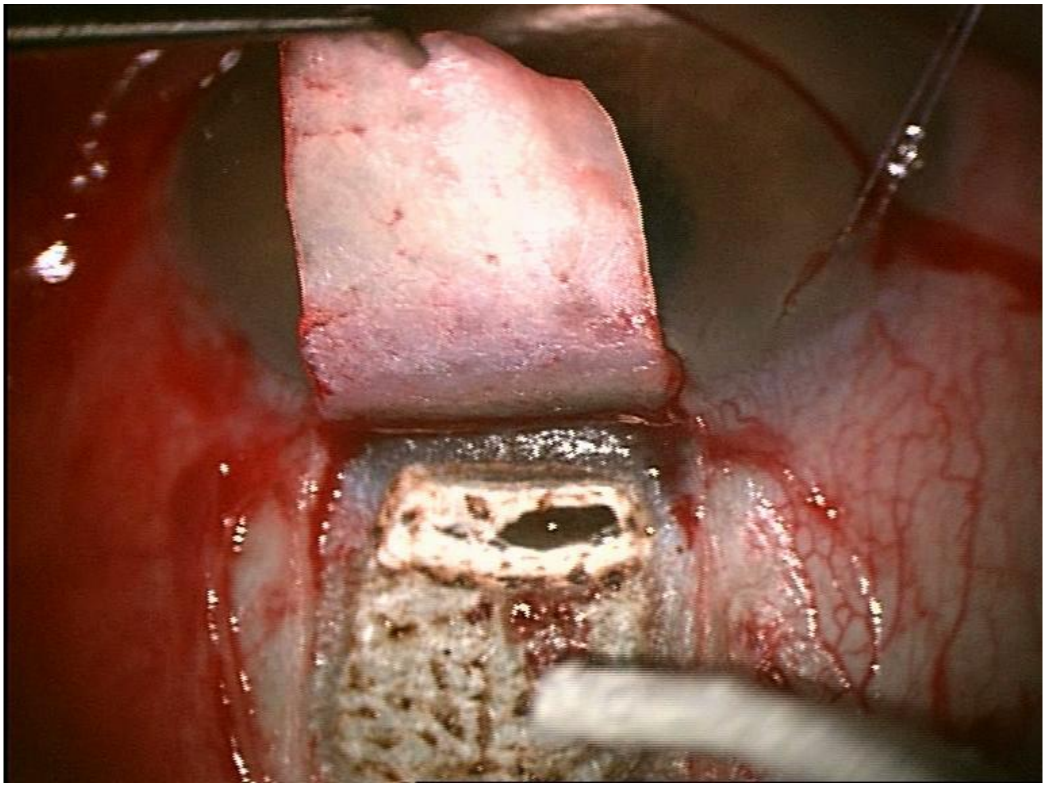

Figure 5.19: Applied CO_2 laser beam over scleral area (including the Schlemm’s canal) with aqueous humor starting to percolate from the anterior chamber. *Private collection of TS, permission granted for use*

6. SUPRACHOROIDAL SHUNT DEVICES:

1. THE SOLX® GOLD SHUNT:

The SOLX® Gold Shunt is a flat device, made of pure gold and measuring 60 microns in thickness and 6 mm in length **(Figure 6.1)**. The shunt is placed via an ab-externo approach (transsclerally). The role of the device is to shift aqueous humor from the anterior chamber into the large supraciliary region. One of the main advantages of this shunt is that a clear cornea is not required for its implantation.[56,57]

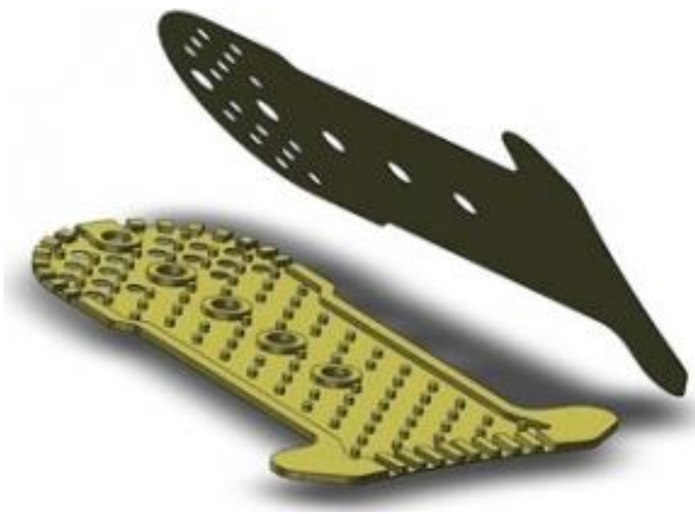

Figure 6.1: Interior view of the SOLX® Gold Shunt. *Loewen N. The Suprachoroidal Space in Glaucoma Surgery. Refractive Eye Care. July 2012.*

2. THE AQUASHUNT™:

The Aquashunt™ (OPKO Health Inc City) is another suprachoroidal device that is placed transclerally through an ab-externo approach **(Figure 6.2)**.

A possible disadvantage of the Aquashunt is its thickness, as the underlying choroid can be easily displaced by the device. However, its large size has to potential to resist long-term fibrosis more effectively than a narrow-bore shunt.[58]

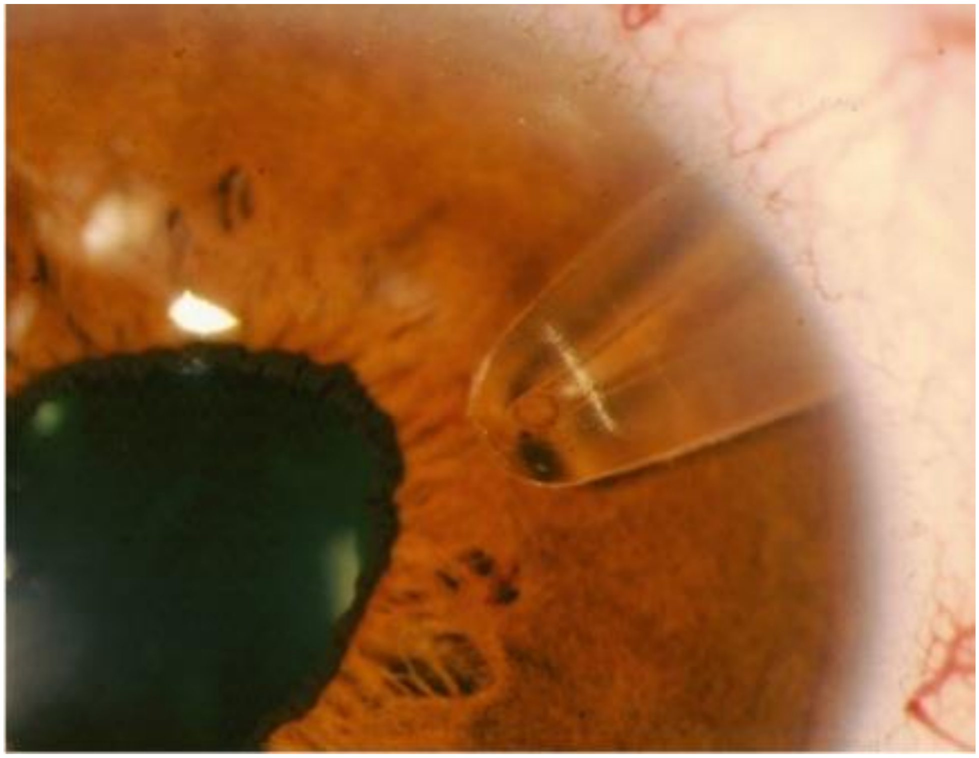

Figure 6.2: The Aquashunt placed transcerally draining aqueous humor from the AC to the suprachoroidal space. *Courtesy of Brian Shields.*

3. THE CYPASS® MICRO-STENT:

The CyPass® Micro-Stent (Transcend Medical) is a long tube made of polymide, 6.35-mm in length with an external diameter of approximately 0.5 mm **(Figure 6.3).** This flexible stent is inserted via a paracentesis through an ab-interno transcameral approach. One of the disadvantages of this device is the need for a clear cornea, as a clear view of the AC angle is essential for its implantation. On the other hand, the CyPass stent can be inserted in conjunction with cataract surgery. Recent studies have demonstrated stable IOP reduction at one year postoperatively, with no complications other than inflammation and transient hypotony in the early postoperative period.[59-60]

Figure 6.3: CyPass® Micro-Stent. *Courtesy of Transcend Medical*

4. iSTENT SUPRA® MICRO-STENT:

Figure 6.4: iStent Supra®. *Courtesy of Glaukos.*

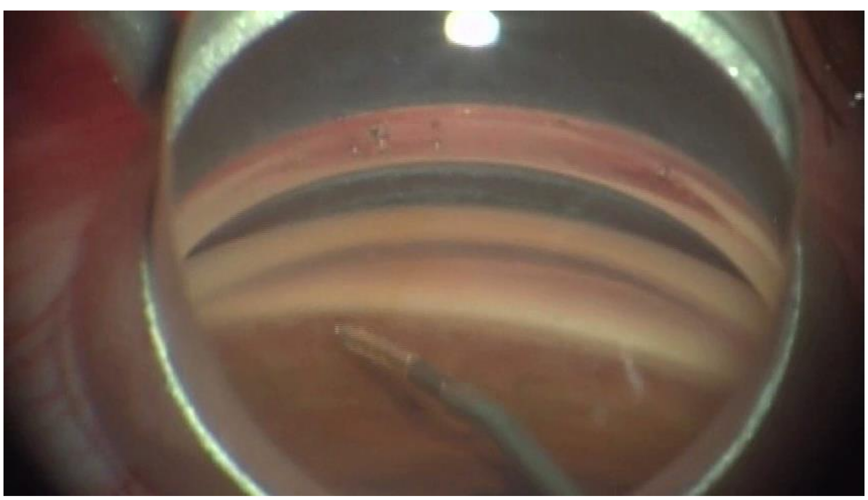

Figure 6.5: Placement of iStent Supra via an ab interno approach into the suprachoroidal space facilitated by a goniolens. *Private collection of TS, permission granted for use*

iStent Supra is another device stent **(Figure 6.4)** which is inserted via an ab-interno approach into the suprachoroidal area with the use of a goniolens. It can be implanted as an isolated procedure or in combination with cataract surgery **(Figure 6.5).** It is the only shunt to have a heparin coating.[61]

5. STARFLO™:

STARflo is a non-degradable implant made entirely from silicone STAR® Biomaterial **(Figure 6.6)**. It is designed to function as a bleb-free device, and reduce fibrotic response, and is used in the reduction of IOP in open angle glaucoma.[57]

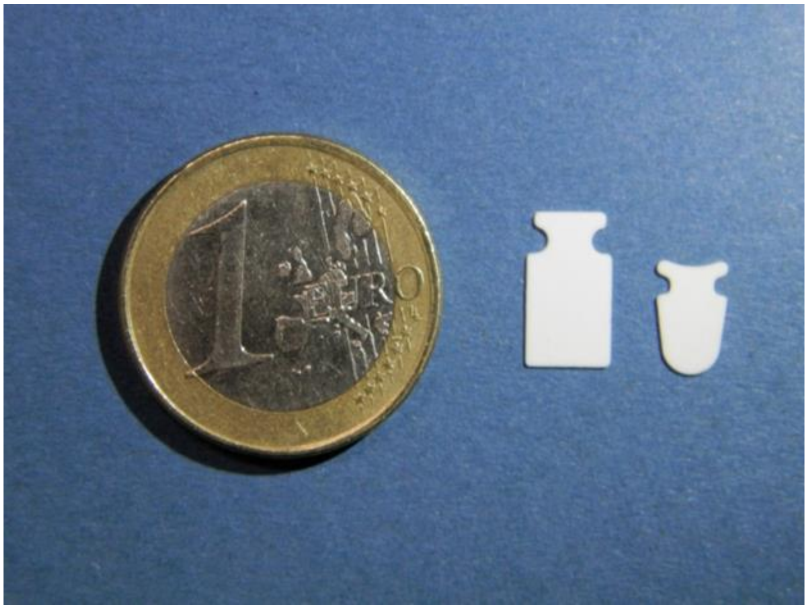

Figure 6.6: STARflo™ suprachoroidal implants (first version, left; second version, right). *Courtesy of iStar Medical*

In a study by Pourjavan et al[62], 4 patients with advanced open angle glaucoma were implanted with STARflo and followed up over a 12 month period. After creation of a conjunctival and superficial scleral flap, an incision in the deep layer of sclera was performed, and the device inserted. The body of the implant was placed in the suprachoroidal space, and the head placed in the anterior chamber. The superfical scleral flap was then tightly sutured. The mean preoperative IOP was 37.0 mmHg and the mean preoperative medication intake was 3.25 per day. Post-operatively after 12 months, 3 of the 4 patients included in the study (the fourth patient was dropped out) had a mean IOP of 14.3 mmHg and mean glaucoma medication intake of 1.5 per day. No intraoperative or immediate postoperative complications were reported. They concluded that the implant showed promising results, but long term follow up was required.

7. MECHANISMS OF FILTRATION OF NPGS:

In patients with primary open angle glaucoma (POAG), the main site of resistance to aqueous outflow is the juxtacanalicular meshwork (JCT) and inner wall of the canal of Schlemm.[63] By eradicating these structures, the outflow facility can be enhanced. The surgically created TDM will form a resistance site to the outflow of aqueous humor, prohibiting sudden decrease of IOP and consequently preventing postoperative hypotony and its complications.[64] Rossier et al[65] reported that the IOP decrease after trabeculectomy was 5.5 times quicker than after DS alone. After passage through the TDM, four possible mechanisms for aqueous absorption may occur; via intrascleral bleb filtration, **(Figure 7.1)**, by suprachoroidal filtration, through a subconjunctival filtering bleb and via Schlemm's canal to the episcleral veins.[66]

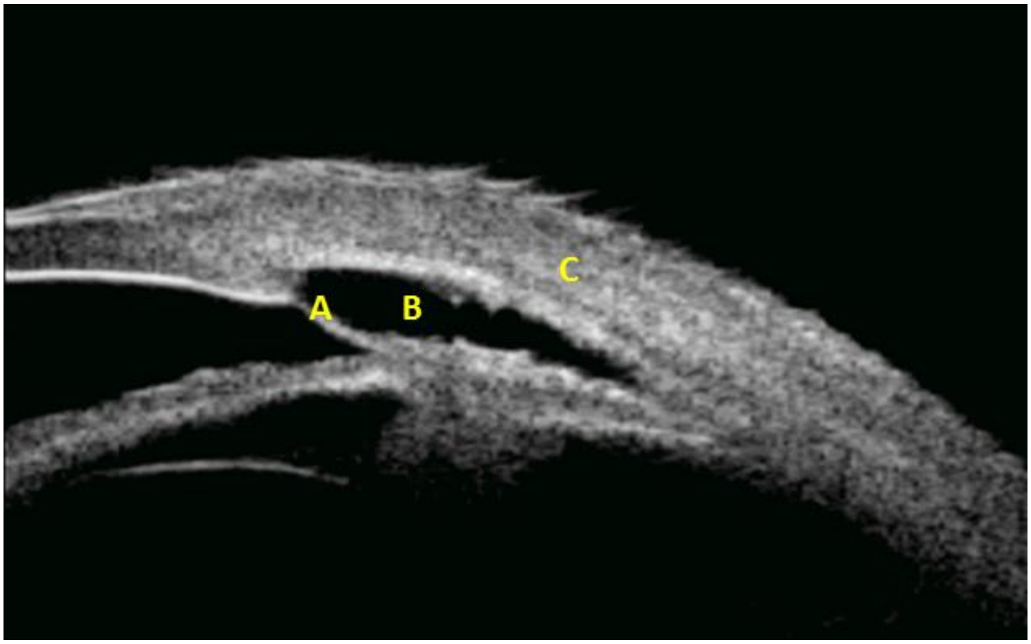

Figure 7.1: UBM image of the TDM (A), intrascleral space (B) and subconjunctival bleb (C) one year after deep sclerectomy with intrascleral collagen implant. *Own private collection*

8. INDICATIONS AND CONTRAINDICATIONS OF NPGS:

A. INDICATIONS:

1) In Open Angle Glaucoma:

NPGS can be an ideal option in the earlier stage of **primary** open angle glaucoma due to its low complication rate compared to trabeculectomy.[63] In addition, the rate of cataract formation with NPGS is less.[67]

In **secondary** open angle glaucoma, NPGS is a safer choice as trabeculectomy is known to have a higher complication rate in eyes with pseudoexfoliation glaucoma (PEXG).[68,69] In pigmentary glaucoma, NPGS targets the pigment-rich TM potentially augmenting aqueous outflow therefore decreasing IOP.[38]

2) Juvenile and Congenital Glaucoma:

NPGS maybe considered as a first line of surgical treatment in cases of juvenile and congenital glaucoma. Numerous studies have reported the efficacy of DS in these types of glaucoma, with a better safety profile than trabeculectomy.[70,71] Viscocanalostomy efficacy and safety was reported by Noureddin et al[72] in patients with newly diagnosed bilateral primary congenital glaucoma. On the other hand, in cases where the AC angle is grossly abnormal, combining DS with other procedures or converting it into a trabeculectomy have been the methods of choice.[73]

3) Uveitic Glaucoma:

In uveitc glaucoma, the high levels of post-operative inflammation and scarring make filtering techniques more susceptible to failure. NPGS can be of benefit in these situations as it is causes much less surgically-induced inflammation than trabeculectomy.[74] Reports in literature demonstrate that viscocanalostomy is a feasible option in eyes with medically uncontrolled uveitic glaucoma.[75] However, if extensive peripheral anterior synechia is present due to recurrent inflammation, NPGS would not be an effective option, as the trabeculum and hence the TDM, would be blocked by inflamed iris tissue.[38]

4) In High Myopic patients:

In trabeculectomy, choroidal detachments can occur in 10-15% of high-myopic glaucoma cases.[76] In a study by Hamel et al[77], complications were reported to be considerably lower with DS.

5) Sturge Weber Syndrome associated Glaucoma:

This syndrome is known to be resistant to medical treatment.[78] Goniotomy and trabeculotomy have little or no role.[79] Trabeculectomy in these cases give fine results but is reported to be susceptible to massive choroidal effusions or expulsive hemorrhage.[80] DS alone, or followed by goniopuncture, has been reported to safely and effectively control IOP. [81]

B. CONTRAINDICATIONS:

Narrow angle glaucoma is considered a **relative** contraindication for NGPS, as in these cases the rate of iris incarceration or anterior synechia is high.[82] NPGS might not be possible in angle-recession glaucoma, as the extensive scarring of the trabeculum render these surgeries ineffective.[38]

An **absolute** contraindication is neovascular glaucoma, as the irido-corneal angle is usually in an advanced stage of peripheral anterior synechia. Trabeculectomy may be tried but in most cases implantation of drainage devices becomes necessary.[83]

9. ADJUNCTIVE PROCEDURE OF NGPS: LASER GONIOPUNCTURE

Indications:

Elevated IOP due insufficient filtration through the TDM.[84]

Procedure:

With the goniolens in place and a power setting of 2-3 mJ, 2-15 shots of Nd:YAG laser are directed towards the corneal side of the TDM to create full thickness holes. To avoid iris incarceration, pilocarpine is prescribed for up to 3 weeks after the procedure. The effectiveness of the treatment depends primarily on how well the dissection of the TDM was carried out during the DS operation **(Figures 9.1–9.3)**.

Figure 9.1: Gonioscopic appearance of TDM after DS, before goniopuncture. *Private collection of AM, permission granted for use*

Figure 9.2: Gonioscopic view of the TDM after goniopuncture. *Private collection of AM, permission granted for use*

Results in Literature:

In one cohort study reported by Shaarawy et al[85], goniopuncture was done in 46% of patients who had undergone DS. In another study, Shaarawy et al[82] reported that 37% of their patients that underwent viscocanalostomy needed goniopuncture in a five-year follow-up. Other studies reported similar results.[81,85-90]

Complications:

Complications as choroidal detachment, and iris synechia and prolapse have been reported.[84,88,89] In the event of iris synechia and prolapse, treatment with Nd:YAG and argon laser synechiolysis and peripheral iridectomy (PI) may be performed.[88,89]

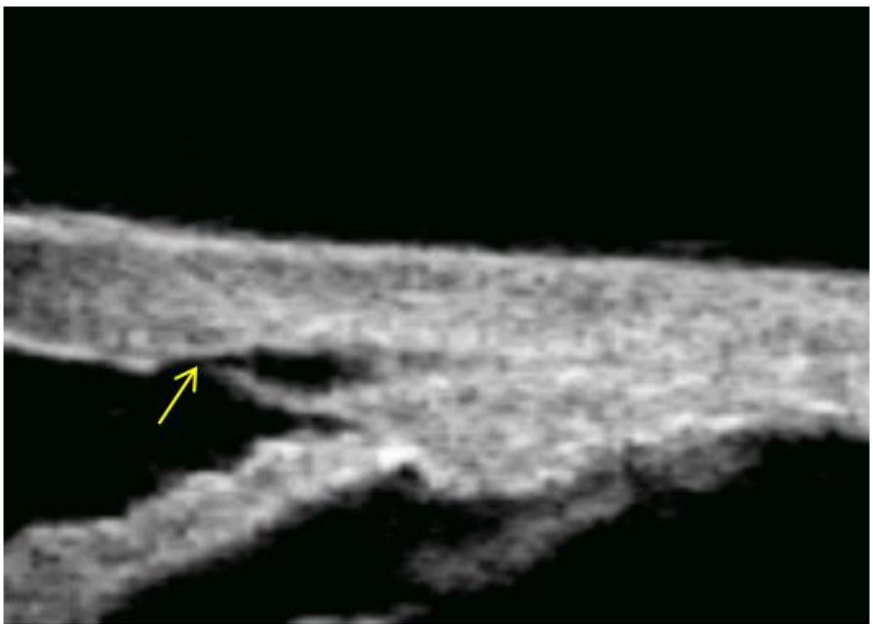

Figure 9.3: UBM image of the TDM after goniopuncture. Yellow arrow pointing towards opening of the TDM. *Own private collection*

10. COMPLICATIONS OF NPGS:

The complications of NPGS are known to be less than trabeculectomy.[8] The sluggish flow of aqueous humor through the TDM prevents an abrupt drop in IOP thus preventing sudden hypotony. In addition, visual acuity is usually more preserved following NPGS than with trabeculectomy as postoperative inflammation levels are lower due to no PI being performed. In spite of this, NPGS is still associated with certain complications that may be intraoperative, early postoperative or late postoperative.[38]

A. INTRAOPERATIVE COMPLICATIONS:

TDM Perforation:

During the early learning phase of deep sclerectomy, TDM perforation is the most common intraoperative complication. Karlen et al[91] reported perforation of 30% of cases during the initial learning period, with this percentage decreasing to 3.1% with increased surgical experience. A study by Sanchez et al[92] also demonstrated the same percentages. The perforation usually occurs between the Descemet‘s membrane and the anterior trabeculum; and such a tear will usually lead to iris prolapse.[37] This complication may also take place during the deep flap dissection when fashioning the TDM.

The management of a TDM perforation varies according to the depth of the AC, the size of the hole, in addition to the presence or absence of a prolapsing iris. The surgery could be continued without interruption in the presence of small sized holes with absence of iris prolapse. In cases of large perforations, or small holes with flat or shallow AC and absence of prolapse, reformation of the AC with viscoelastic material should be performed. In such scenarios the flap should be sutured tightly. In case of an iris prolapse accompanying a large defect, converting NPGS to a penetrating surgery (trabeculectomy) by performing a peripheral iridectomy is the best course of management; and in these cases, the superficial flap should also be well sutured and viscoelastic material could be injected under to impede to aqueous outflow thus minimizing the incidence of postoperative hypotony.[38]

B. EARLY POSTOPERATIVE COMPLICATIONS:

1) Bleb and Wound Leaks:

Wound leaks (positive Seidel test) occur in NPGS just as common as in trabeculectomy[70] and are often due to inadequate closure of the conjunctiva.[93] Usually the leaking stops spontaneously within a few days.[38]

2) Inflammation:

Inflammatory reaction after NPGS can occur, however it is less than trabeculectomy.[70]

3) Hypotony:

Hypotony in the immediate postoperative period may occur for a few days but usually with a well-formed anterior chamber.[9] It is considered a positive indicator for long-term IOP control on. In the event of persistent hypotony (which is uncommon), hypotonic maculopathy can occur, similar to trabeculectomy.[9]

4) Descemet's Membrane Detachment:

Descemet's membrane (DM) detachment, although rare, can occur after NPGS[94,95] **(Figure 10.1)**. This complication might take place as a result of aqueous humor passage into the plane above the DM secondary to an increase the pressure inside the bleb; which may occur after trauma or in case of an encysted bleb or following ocular massage.[37] In case of an extensive intra-corneal hematoma obscuring vision, immediate descemetopexy should be carried out. Another surgical approach is to perform a break in Descemet's membrane, followed by air and balanced salt solution injections into the AC to wash out the hematoma; and promote reattachment by injecting a long lasting gas.[96]

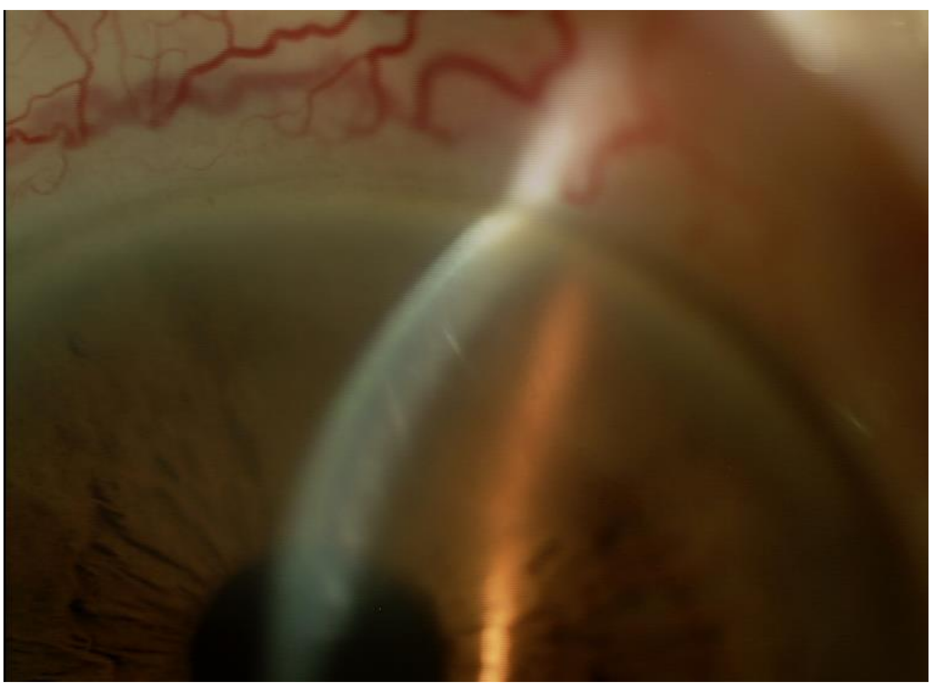

Figure 10.1: Descemet's membrane detachment post-DS. *Private collection of AM, permission granted for use*

5) Infectious Keratitis:

A single case of Staphylococcus aureus keratitis was detected in a case 2 weeks post-DS without the use of antimetabolites.[97] Fungal keratitis was reported in one patient 7 days after NPGS.[98]

6) Blebitis:

Blebitis is a grave condition that can cause blindness. It can occur following both trabeculectomy and NPGS and lead to endophthalmitis[99,100] **(Figure 10.2)**. The TDM is said to form a barrier against the spread of microbes in NPGS, so hypothetically endophthalmitis happens less with NPGS.[101,102] In a case report by Chiseliţã and Danielescu[102], one case of bleb-related endophthalmitis was discovered 2 months post-DS. Severe retinal necrosis and visual loss was the end result of this case.

Figure 10.2: Blebitis leading to endophthalmitis post-DS. *Private collection of AM, permission granted for use*

7) Early Postoperative Rise in IOP:

Resistance of outflow after NPGS is mainly located at the TDM, therefore inadequate or insufficient surgical dissection of the membrane may be the main cause of early postoperative increase in IOP.[103] This should not occur if the TDM was fashioned in the correct manner. High IOP due to tight sutures as in trabeculectomy is uncommon. Residual viscoelastic in the AC may cause a rise in IOP postoperatively, as well as hemorrhage remaining in the scleral bed (which normally resorbs spontaneously within a few days). Peripheral anterior synechia (at the site of the TDM) can sometimes occur following intraoperative micro-perforation of the TDM, leading to an IOP spike.[38] Eye rubbing or straining might cause late TDM rupture with iris prolapse which may lead to elevated postoperative IOP.[104] Management consists of miotic eye drops and Nd:YAG laser synechiolysis. Surgical iridectomy may be indicated in conditions not responding to medical therapy.

C. LATE POSTOPERATIVE COMPLICATIONS:

1. Fibrosis of Conjunctival Bleb:

Conjunctival fibrosis is the main cause of bleb failure.[38] Early signs of this complication include raised IOP, diffuse conjunctival injection and the appearance of large tortuous vessels. This condition is slightly less frequent in trabeculectomy than with NPGS.[38] Management consists of needling procedure combined with subconjunctival injections of an antimetabolite, and/or GPT.[38]

2. Iris Prolapse and Synechia:

Blunt trauma, eye rubbing, or coughing may result in a TDM tear with subsequent iris prolapse.[105] This condition may also occur after intraoperative micro perforation of the TDM or YAG laser goniopuncture[89] **(Figure 10.3)** Medical treatment and laser synechiolysis could be attempted to retract the iris. In case of failure, surgical intervention could be necessary, especially in cases of increased IOP.[105]

3. Corneal Astigmatism and Endothelial Cell Loss:

NPGS appears to have low levels of loss of endothelial cells with less effect on corneal astigmatism.[106] In addition, Arnavielle et al[107] concluded that endothelial cell damage is significantly less after DS than with trabeculectomy.

4. Scleral Ectasia:

Milazzo et al[108] reported a case of scleral ectasia 3 weeks post-DS in a patient with glaucoma secondary to chronic uveitis (from chronic juvenile idiopathic arthritis).

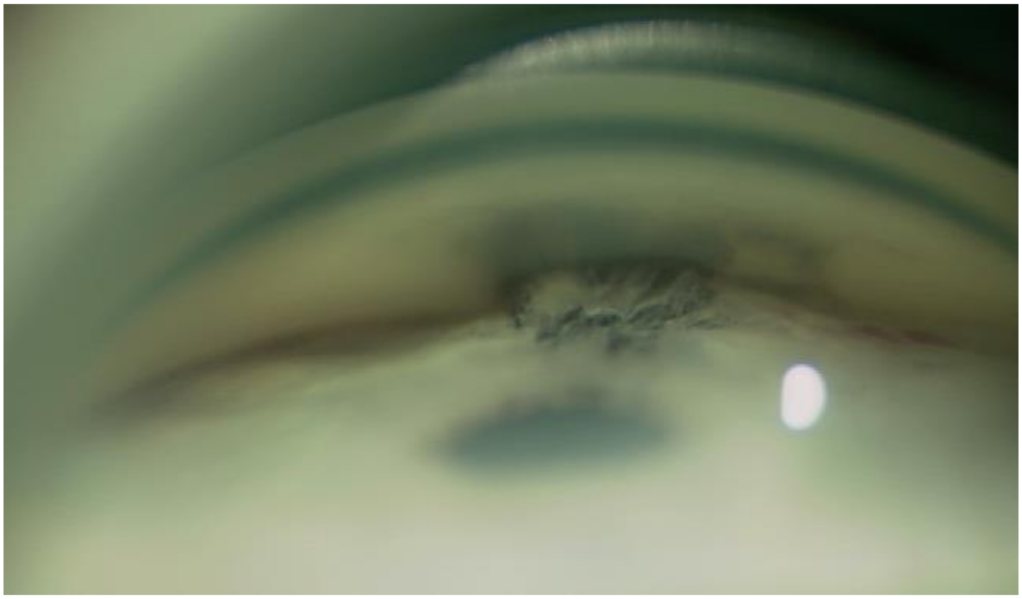

Figure 10.3: Iris incarceration in the TDM, post-goniopuncture. *Private collection of AM, permission granted for use*

11. RESULTS OF NGPS IN LITERATURE:

A. DEEP SCLERECTOMY WITHOUT IMPLANTS:

Table 11.1: Results of previous studies of DS without implant.

STUDY	RESULTS
Bas et al[109]	Mean IOP reduction 40% after 6 months
Massy et al[110]	Success rate was 81% (target IOP at 21 mm Hg) and 50% (target IOP at 16 mm Hg) at 18 months
Dahan et al[111]	Mean IOP reduction 50% at 46months
Kozobolis et al[112]	Complete and qualified success rates were 42.5% and 72.5% in the DS group and 50% and 95% in the DS-MMC group
Yamin et al[113]	Mean IOP reduction 35% after 9.5 months
Dahan et al[114]	Mean IOP reduction of 62% +/- 6% in the implant group versus 34% +/- 13% in the DS without implant group
Guedes et al[115]	Complete success was 82.7% and relative success was 93.3%. at 20 month
Shaarawy et al[85]	Complete success rate was 38% for the DS group and 69% for the DSCI group. Qualified success rate was 69% and 100% for the DS and DSCI groups at 48 months, respectively
Mielke et al[116]	Complete success rates (IOP< 18 mm Hg) at 1 year was 70% and 79%, and at 18 months was 35% and 38% for the DS-no MMC and DS-MMC groups, respectively. Qualified success was 65% and 73% at 1 year, and 24% and 13% at 18 months for the DS-no MMC and DS-MMC groups, respectively
Khairy et al[117]	Surgical success rates (IOP was less than 22 mm Hg and the IOP was reduced greater than 20% without the use of any medication.) at 12, 24, and 30 months were 61.4%, 36.6%, and 18.9%, respectively
Al Obaidan et al[118]	Complete success was 82%, while overall success was 90.2%.at 60.9 (+/-49.7) months
Anand and Bong[119]	Complete success rates of 87.5% at 1 year and 74.4% at 2 years after DS-MMC groups

B. DEEP SCLERECTOMY WITH IMPLANTS:

I. Implant in the Intrascleral Space:

Table 11.2: Results of studies with DS with intrascleral implant.

STUDY	RESULTS
Demailly et al[120]	Complete and qualified success at 16 month was 75.6% and 79%
Welsh et al[121]	IOP lower than 21 mm Hg in 88.9% of their patients at 3 to 6 months postoperatively and in 87.5% of the patients at 6 to 12 months
Bissig et al[122]	Complete and qualified success at 102 month was 47.7% and 89%
Mendrinos et al[123]	Complete and qualified success rates were 54.5% and 90.9%, at 54 month
Shaarawy et al[85]	55.4 % reduction at 48 month

II. Implant in the Suprachoroidal Space:

Table 11.3: Results of studies of DS with suprachoroidal implant.

STUDY	RESULTS
Mużoz[13]	Complete success rate at 1 year was 73.8% (IOP <22mm Hg without medication) The qualified success rate at 1 year was 93.4% (IOP <21mm Hg with or without medication)
Bonilla et al[124]	23 eyes underwent combined phacoemulsification and DSSCI. At 12 months, complete success was 45%, qualified success was 95%, and the failure rate 5%.

C. VISCOCANALOSTOMY:

Table 11.4: Results of studies on Viscocanalostomy.

STUDY	RESULTS
Stegmann et al[30]	Complete success of 82.7% and qualified success of 89% at 35 months
Shaarawy et al[82]	Complete success of 60% and qualified success of 90% at 60 months
David et al[125]	Complete success of 54% and qualified success of 82%at 60 months
Moradian et al[126]	Complete success of 71% and qualified success of92.4% at 1 year

D. CANALOPLASTY:

Table 11.5: Results of studies on Canaloplasty.

STUDY	RESULTS
Peckar & Korber[127]	Complete success of 83% and qualified success of 87% at 3year
Grieshaber et al[128]	Complete success of 77.5% and qualified success of 81.6% at 36 M
Grieshaber et al[129]	Complete success of 93.8% at 12 month
Lewis et al[130]	IOP reduction of 35 7% at 36 month
Ayyala et al[131]	IOP reduction of 32% at 12 month
Koerber[132]	IOP reduction of 45 % at 18 month
Barnebey[133]	IOP reduction of 43% at 12 month

12. ULTRASOUND BIOMICROSCOPY (UBM):

Pavlin et al[19,20] in the early 1990s developed this technique by using high-frequency ultrasound (50–100 MHz) to provide high-resolution (20–60µm) imaging of ocular structures in the anterior segment. It's a contact method which allows precise measurements of the anterior segment tissues. Even though slit lamp evaluation of filtering blebs is useful for identifying signs of subconjunctival bleb evolvement, it is a subjective method. In addition, the intrascleral blebs and/or the suprachoroidal space cannot be seen or evaluated by this mode of examination.[134]

Recently, UBM has been used to analyze filtering bleb morphology after glaucoma surgery.[21] It allows the visualization of the operated region; enabling measurement of the dimensions of the intrascleral cavity, the thickness of the TDM, presence or absence of a suprachoroidal space and the morphology of the subconjunctival bleb[135] **(Figure 12.1)**. It also allows visualization of structural alterations caused by filtrating surgery, aiding in understanding its mechanism of action and the anatomical causes of failure.[136]

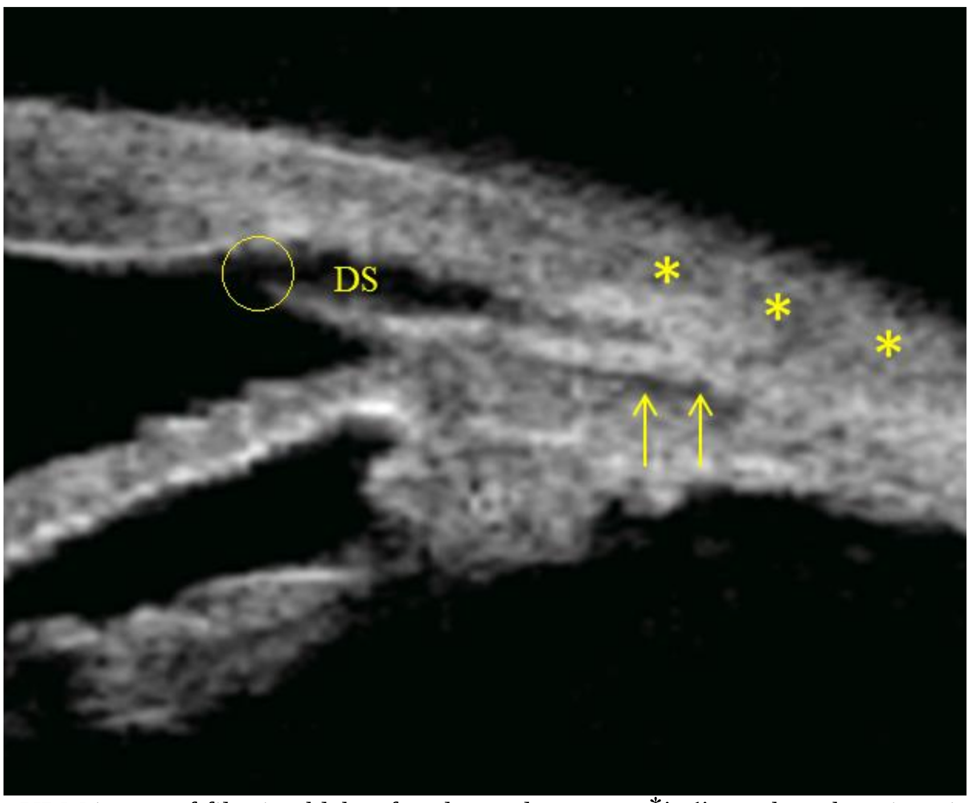

Figure 12.1: UBM image of filtering blebs after deep sclerectomy.*indicate the subconjunctival bleb; DS, decompression (intrascleral) space; circle, GPT-opened TDM; arrows, suprachoroidal space. *Own private collection*

RESULTS IN LITERATURE FOR EVALUATION OF BLEB MORPHOLOGY IN NPGS WITH UBM:

Table 12.1: Results of studies of UBM analysis of NPGS.

STUDY	RESULTS
Chiou et al[21]	9 eyes underwent deep sclerectomy with intrascleral collagen implant (DSCI). A hypoechoic area in the suprachoroidal space was seen in 4 cases (44%). Mean TDM thickness was 110.1 (16.8) microns, 1 month postoperatively
Chiou et al[137]	Study of 45 eyes with DSCI. In 23 eyes (51%), a hypoechoic area in the suprachoroidal space was seen. The mean thickness of the trabeculo-descemetic membrane was 0.13 mm ± 0.02. The collagen implant dissolved slowly within 6 to 9 months, leaving an intrascleral cavity
Marchini et al[11]	Study of 30 eyes with DS with RHAI. At 12 months, a subconjunctival filtering bleb was found in 18 patients (60%), a supraciliary hypoechoic area in 18 (60%), and hyporeflective scleral tissue around the intrascleral space in 14 (47%). Higher surgical success rate significantly correlated with the presence of all three feature simultaneously in the same eye (P=0.004)
Kazakova et al[135]	Study of 43 eyes, DSCI. Forty eyes showed clinically a diffuse filtering bleb, with a subconjunctival space in all eyes. Intrascleral space detected in 39 eyes (92.8%). The mean volume of this space was 1.8 (range 0.11-6.53) mm^3. Supraciliary hypoechoic area detected in 19 eyes (45.2%)
Khairy et al[138]	Study of 22 eyes, DS with no implant. At 12 months, poor correlation between IOP and the dimensions of intrascleral or the thickness of remaining TDM. Surgical success was not correlated with presence and type of filtering bleb
Contreras et al[40]	DS with an intrascleral Esnoper implant. At 12 months, all three patients had an intrascleral space on UBM. Hyperechogenic implant was seen in all eyes.
Aptel et al[134]	Study of 15 eyes, DSCI. Bleb height and low TDM thickness correlated with lower IOP, at 12 weeks postoperatively.
Cabrejas et al[139]	Study of 18 eyes, DS with intrascleral Esnoper implant. Significant correlation of lower IOP with hyporeflective blebs, with the presence of hyporeflective suprachoroidal space and hyporeflective area around the decompression space. The presence of all 3 filtration signs together correlated with lower IOP levels compared with the presence of only 1 or 2. Lower postoperative IOP significantly correlated with a thinner TDM at 1 month.
Negri-Aranguren et al[86]	Study of 23 yes, with VC. Subconjunctival bleb detected in one eye. All eyes had an intrascleral cavity. Intrascleral space showed no change from 7 to 9 months.
Roters et al[140]	Study of 15 eyes, with VC. Dimensions of decompression space (mean of 0.62 mm^3) did not correlate with IOP, and when absent, control of IOP was not achieved. Normal thickness of the TDM (0.10-0.15 mm) correlated with surgical success.

13. STUDY:

MATERIALS AND METHODS:

The study is divided into **two** sections: **(i)** a prospective, non-randomized, controlled, multicenter evaluation of the safety and efficacy of DSSCI **(ii)** prospective, non-randomized, single center controlled study to evaluate bleb morphology of DSSCI after one year.

The study was carried out in Switzerland in accordance with the Declaration of Helsinki. An informed consent document was signed by all the patients before the start of the study. The clinical trials were performed in the Glaucoma Sector at Geneva University Hospital (HUG), and in the Glaucoma Department at Clinique de Montchoisi in Lausanne. 28 eyes were included in this study; 15 eyes from the Clinique de Montchoisi, and 13 from the HUG. Inclusion and exclusion criteria are displayed below in **Table 13.1**.

Table 13.1: Patient inclusion and exclusion criteria.

INCLUSION CRITERIA	EXCLUSION CRITERIA
1. ≥21 years. **2.** Primary or secondary open angle glaucoma. **3. P**hakic or pseudophakic eyes with no ocular disorder besides cataract, and no prior intervention but cataract surgery and/or trabeculoplasty performed > 3 months prior to study enrollment. **4.** Medically uncontrolled IOP. **5.** Patients agreed to sign written informed consent prior to study participation. **6.** Patients were ready, willing and able to undergo post-operative follow-up requirements.	**1.** Any other type of glaucoma other than primary or secondary open angle glaucoma. **2.** Previous surgery performed in the study eye besides cataract; and history of ophthalmic laser procedures besides laser trabeculoplasty. **3.** Optic neuropathy other than glaucoma, and history of severe eye trauma in the study eye. **4.** Dense corneal opacification which may deny satisfactory optic disc evaluation in the study eye. **5.** Patient with severe retinopathy in either eye, history of prior vitrectomy or vitreous hemorrhage in the study eye. **6.** Retinal artery or vein occlusion in the study eye. **7.** Patient with ocular malformations in the involved eye. **8.** Documented congenital anomaly of the angle of the AC in the experimented eye. **9.** Concurrent infective/ inflammatory ocular eye disease in the study eye **10.** Patient suffering from severe or disabling systemic disease. **11.** Participating in another clinical trial. **12.** Pregnant or breast feeding patient.

All surgeries carried out at the Clinique de Montchoisi were performed by one surgeon, Professor André Mermoud (AM); and at the HUG, by Dr. Tarek Shaarawy (TS) alone. The 9 eyes that underwent UBM imaging were all performed at the Clinique de Montchoisi. The reason to why UBM imaging was performed only on the eyes that underwent surgery at the Clinique de Montchoisi was due to the fact that each center has a different UBM machine; and to ensure a uniform method of imaging and avoid any discrepancies that may arise by examining patients with two different devices, the collaborators of this study concluded that it was necessary to use only one machine. They did not feel this would be an issue by having the surgeries performed by two different surgeons. And the explanation for why 6 of the 15 patients that had the surgery at the Clinique de Montchoisi did not undergo UBM imaging was because some of them refused to come for another visit and the others did not show up for their UBM imaging appointment.

Preoperative Evaluation:

Data collection included demographic information, type of glaucoma, and number of anti-glaucoma medications. All the patients were completely examined preoperatively including:

- Measurement of the best corrected visual acuity (BCVA) with ETDRS chart
- Slit-lamp biomicroscopic examination.
- Gonioscopy.
- Intraocular pressure (IOP) measurement with Goldman tonometer (mean of 3 measurements).
- Fundus examination of the retina and optic nerve head.
- Visual field examination with Octopus 101 dG2 perimeter.

Surgical Procedure:

The surgeries were carried out under subconjunctival and/or retrobulbar local anesthesia by two experienced surgeons; Professor André Mermoud (Clinique de Montchoisi) and Dr. Tarek Shaarawy (HUG). Both surgeons collaborated to make sure they used the same exact surgical technique; utilizing the same collagen device and implanting it in the exact same manner.

To expose the sclera, a fornix-based conjunctival incision was performed. Mild cauterization of the episcleral vessels with a diathermy at the targeted surgical site was carried out. A limbal-based 5 × 5 mm superficial scleral flap was dissected at a depth of about 30% scleral thickness, extending approximately 1 mm forward into clear cornea. Mitomycin 0.02% was applied for 2 minutes on the scleral bed (between the sclera and the Tenon's capsule) followed by irrigation with balanced salt solution. A second (deep) scleral flap was created by dissecting 4 × 4 mm into the bed of the first dissected scleral flap. Further anterior dissection of the deep scleral flap was performed to 'unroof' the canal of Schlemm; with an extra 1 mm of anterior dissection to eradicate the sclerocorneal tissue over the anterior trabeculum and Schwalbe line, creating the thin TDM **(Figure 13.1)**.

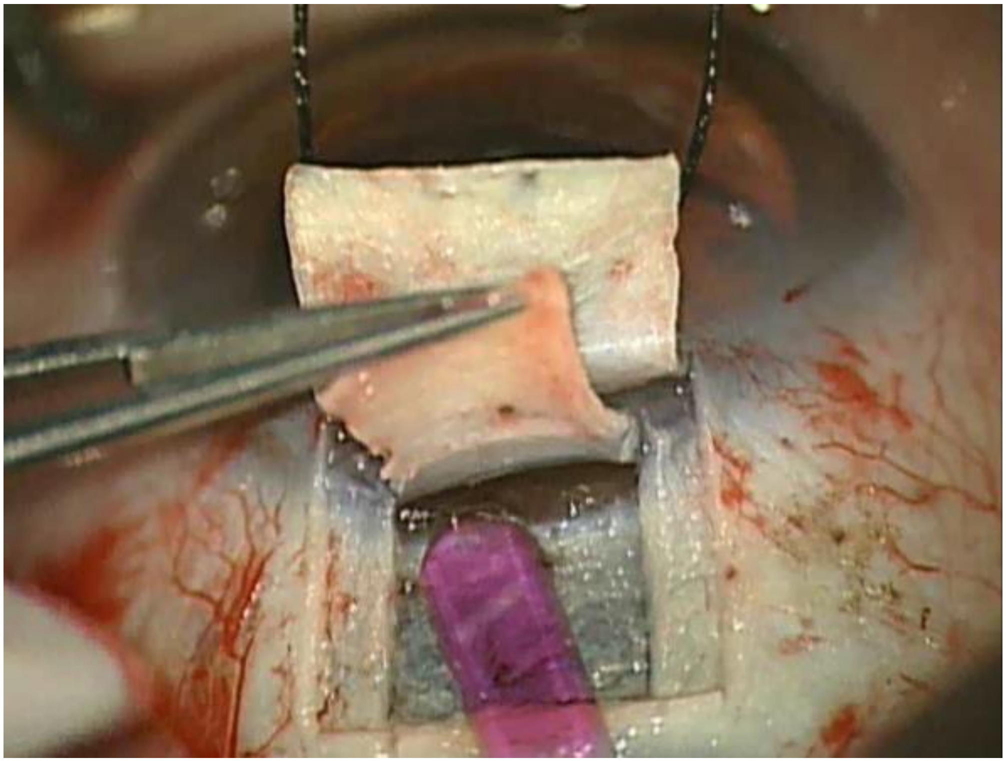

Figure 13.1: Anterior dissection of the deep scleral flap into the corneal tissue to create the TDM. *Private collection of AM, permission granted for use*

With the use of scissors, the hinge of the deep scleral flap was cut and removed **(Figure 5.3)**. At this step, aqueous humor percolation through the TDM could be seen. The juxtacanalicular trabeculum and endothelium of the canal of Schlemm were then removed using a small blunt forceps **(Figure 5.5)**. A horizontal incision 1.5-2 mm is made in the remaining deep scleral bed, about 1 mm posterior to the scleral spur, creating a sub-scleral pocket **(Figure 13.2)**. An Aquaflow collagen implant **(Figure 5.9)** was then placed in this pocket in the underlying suprachoroidal space. About one-half to two-thirds of the implant is placed into this pocket, the remaining part in the intrascleral cavity **(Figure 13.3)**. Suturing of the superficial scleral flap is carried out with 10/0 nylon sutures, followed by the conjunctiva with 8/0 vicryl sutures **(Figure 13.4)**.

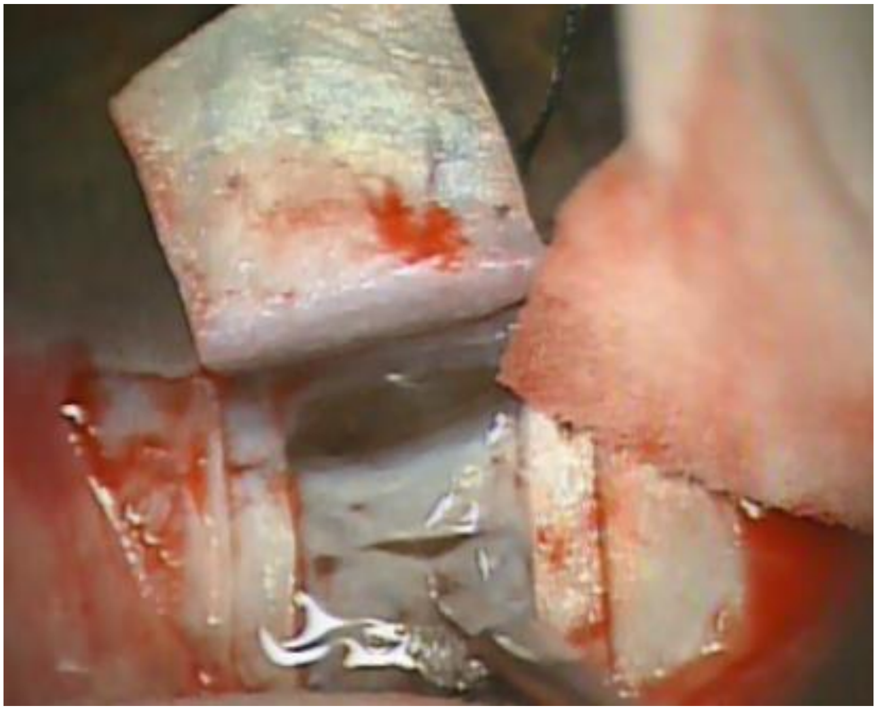

Figure 13.2: Horizontal incision in the remaining deep scleral tissue creating a sub-scleral pocket for insertion of the collagen implant. *Private collection of AM, permission granted for use*

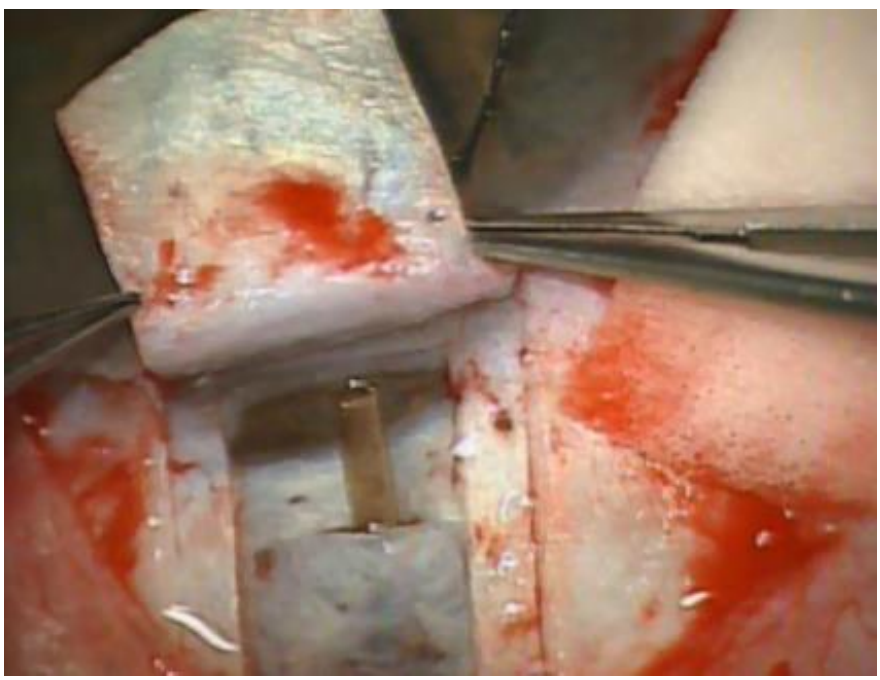

Figure 13.3: Collagen implant inserted through the horizontal incision and into the suprachoroidal space. *Private collection of AM, permission granted for use*

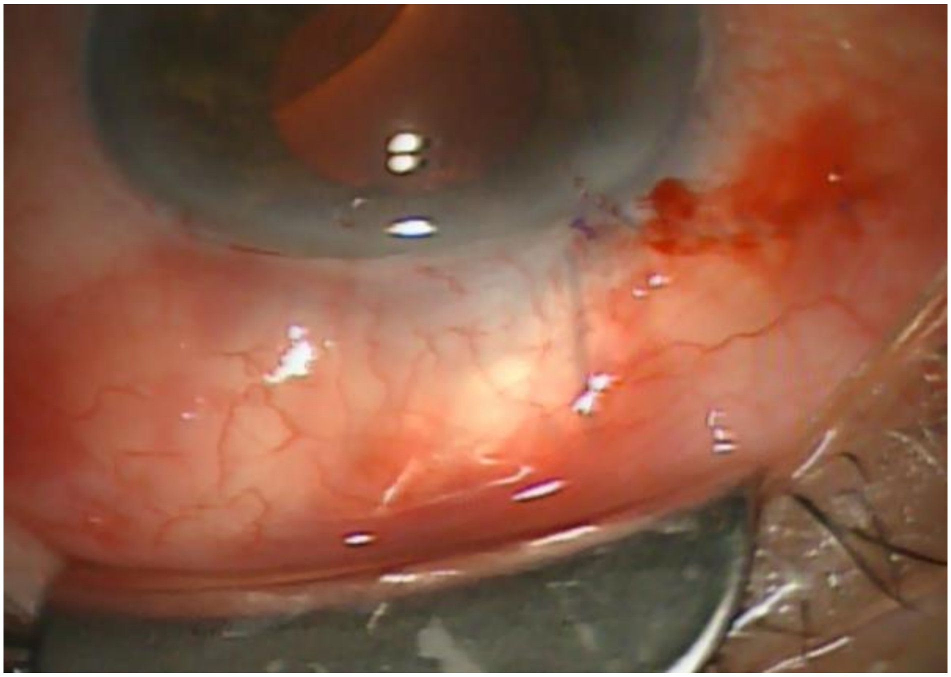

Figure 13.4: External appearance after completion of DS. *Private collection of AM, permission granted for use*

Intraoperative Evaluation:

Occurrences of any intraoperative adverse events were documented.

Postoperative Evaluation:

- Follow-up examinations were performed on the first day postoperatively, at week 1, at months 1, 3, 6 and 12.
- Anterior segment slit-lamp examination, IOP measurement (mean of 3 measurements) and funduscopy was performed at each visit.
- UBM imaging of the anterior segment and filtering blebs was done once at 12 months.
- Any adjunctive procedures carried out as goniopuncture and needling were noted, with measurement of IOP before and after the procedure recorded.
- Any adjunctive anti glaucomatous medications used were also documented.

Postoperative Analysis:

Complete success rate at 12 months was defined as the percentage of patients with IOP ≤ 21 mmHg **without** the use of anti-glaucoma medications and with or without adjunctive procedures

(GPT and/or needling); and qualified success was classified as proportion of patients whose IOP was ≤ 21 mm Hg **with or without** hypotensive therapy. Failure was characterized as patients with IOP ≥21 mm Hg under glaucoma therapy, with the condition needing another filtering procedure, lost light perception or developed phthisis bulbi. The number of ocular IOP lowering medications used by each patient at 12 months was compared with the baseline values.

UBM Imaging Procedure and Analysis:

UBM device:

The Ultrasound Biomicroscope Model BHF-50 Lin (Aviso, Quantel Medical, France) with a 50 MHz transducer was used.

Procedure:

All 9 eyes that underwent UBM imaging were performed (by myself) at the Clinique de Montchoisi, at 12 months postoperatively. Patients were placed in the sitting position. Topical anesthetic drops were instilled in the examined eye. Only one operator performed the imaging procedures for all of the studied eyes. The device was calibrated at a gain of 100dB. The probe was placed on the globe in a perpendicular manner, and fine movements were carried out to analyze the target sites in both transverse (parallel to the limbus) and longitudinal (radial or anteroposterior) scans.

Analysis:

The following features were analyzed:

- Presence of subconjunctival filtering bleb. The blebs were graded as 1 of 4 types: low reflective **(Figure 14.7)**, high reflective **(Figure 14.11)**, encapsulated **(Figure 14.9)**, and flat **(Figure 14.8)**.[11]
- Presence and dimensions of an intrascleral space (IS) under the scleral flap.
- Thickness of the residual TDM.
- Presence of a hyporeflective (supraciliary) suprachoroidal space.

The imaging parameters selected for the present study were established in earlier studies.[11]

Measurement of Dimensions:

Measurement of the dimensions of intrascleral space and thickness of the TDM were done using the caliper installed in the UBM Aviso operating system **(Figures 13.5-13.6).**

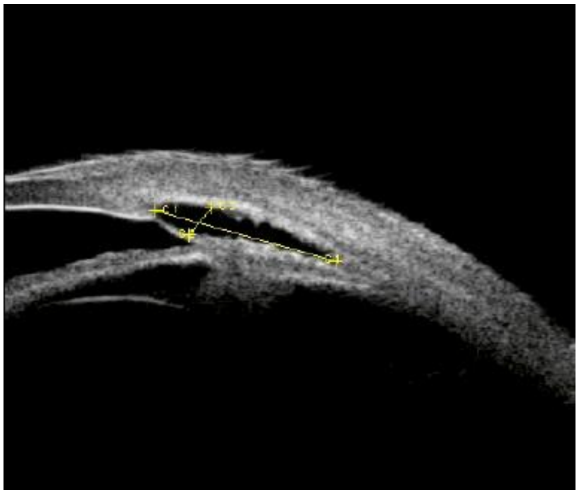

Figure 13.5: UBM image taken in the longitudinal axis (90°) of the deep sclerectomy site. The yellow straight lines indicate the height and length of the intrascleral space, measured using the calipers in the Aviso machine. *Own private collection*

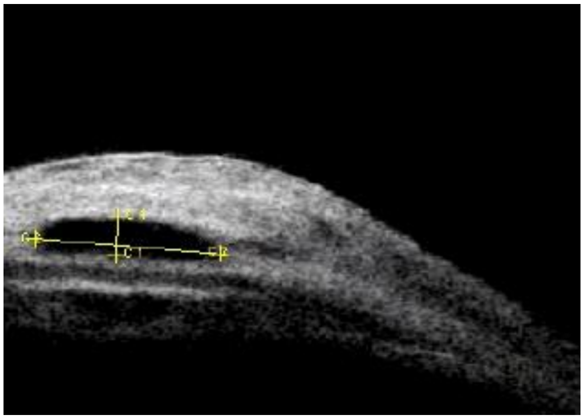

Figure 13.6: UBM image taken in the transverse axis (180°). Height and width of the intrascleral space are measured. *Own private collection*

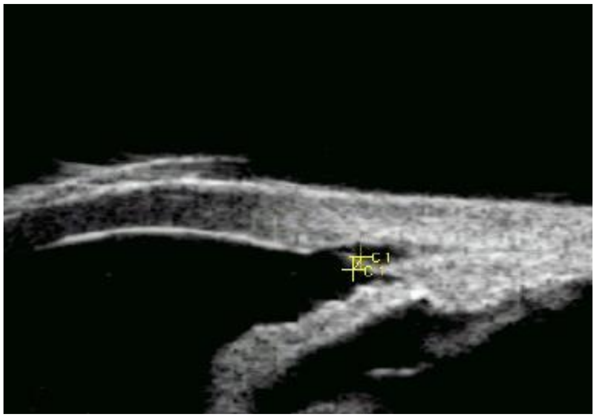

Figure 13.7: Measurement of thickness of TDM (image taken in the 90° axis). *Own private collection*

Estimation of Volume of Intrascleral Space:

As the intrascleral space has an appearance roughly resembling a triangular-shaped prism[11], estimation of its volume (V) can be achieved **(Figure 13.8)**. Maximum length (L) multiplied by maximum height (h) multiplied by maximum breadth (b) divided by 2 (or multiplied by 0.5). **V=0.5(L x h x b)]**.

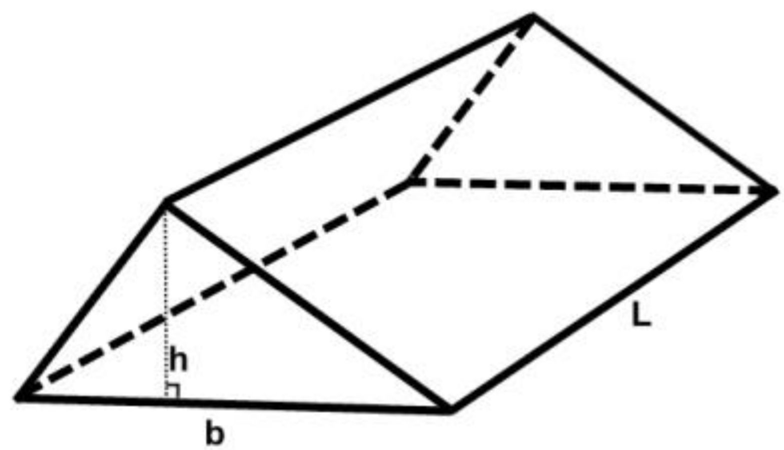

Figure 13.8: Dimensions of a triangular prism. *Own private collection*

Statistical Methods:

A paired t-test was employed to evaluate the significance of IOP changes. At 12 months, the mean IOP measurements and success rates were calculated. P value of <0.05 was considered significant. SAS software (SAS Institute, Cary, North Carolina) was used for the data analysis.

14. RESULTS:

The study included twenty-seven consecutive patients **(28 eyes)** who conformed to the inclusion and exclusion criteria. Demographic data and diagnosis are summarized in **Table 14.1**.

PATIENT DEMOGRAPHICS:

Table 14.1: Demographics, diagnosis and preoperative measurements.

	RESULTS
Number of Eyes	28
Sex (Male %)	25% (7/28)
Age (Mean ± SD)	77.25 ± 7.6
Diagnosis No. %	POAG 39.3 % (11/28); PEX 60.7% (17/28)
Preoperative BCVA (Mean ± SD)	0.76 ± 0.27
Preoperative IOP (Mean ± SD)	24.0 ± 5.8 mmHg
Number of Preoperative Medications (Mean ± SD)	2.56 ± 1.07

SAFETY ANALYSIS:

Intraoperatively:

All 28 surgeries were carried out without any complications. Creation of the TDM took place smoothly without development of perforations or micro-perforations; therefore, none of the cases had to be converted to trabeculectomy with performance of a peripheral iridectomy. Insertion of the collagen implant in the suprachoroidal space was executed without difficulty, and without any adverse events.

Postoperatively:

A single case (3.6%) suffered from hyphema (2 mm level) at day one, and spontaneous resolution occurred without treatment. At day 80, in another case (3.6%), ciliary body (CB) detachment developed with subsequent severe hypotony. The patient was observed, and without any specific treatment, reattachment of the CB took place. There were no reports of bleb leaks (positive Seidel), inflammatory reactions to the collagen implant or iris incarceration into the TDM.

PERFORMANCE ANALYSIS:

At 12 months, the mean preoperative IOP of 24.0 ± 5.8 mmHg dropped to 11.7 ± 2.6 mmHg **(Figure 14.1)**. Therefore, at 12 months, there was an IOP reduction of 51.4% ($P<0.001$) **(Figure 14.2).**

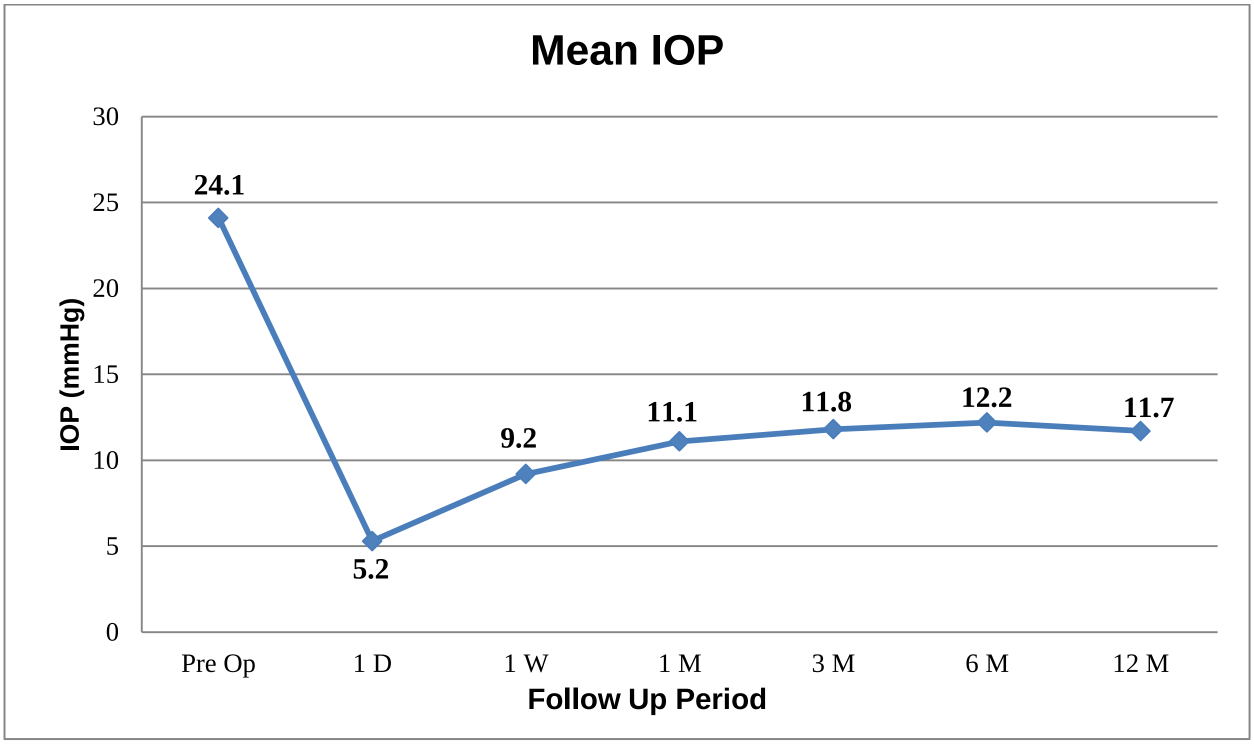

Figure 14.1: Average IOP (mmHg) over 12 month period.

The average BCVA before surgery was 0.76 ± 0.27; and it slightly improved at 6 months to 0.78 ± 0.23, and at 12 months to 0.82 ± 0.23 ($P<0.001$) **(Figure 14.2)**.

Patient hypotensive medications usage decreased from an average of 2.57 ± 1.07 preoperatively to 0.29 ± 0.53 at 6 months, and 0.18 ± 0.39 at 12 months ($P<0.001$).

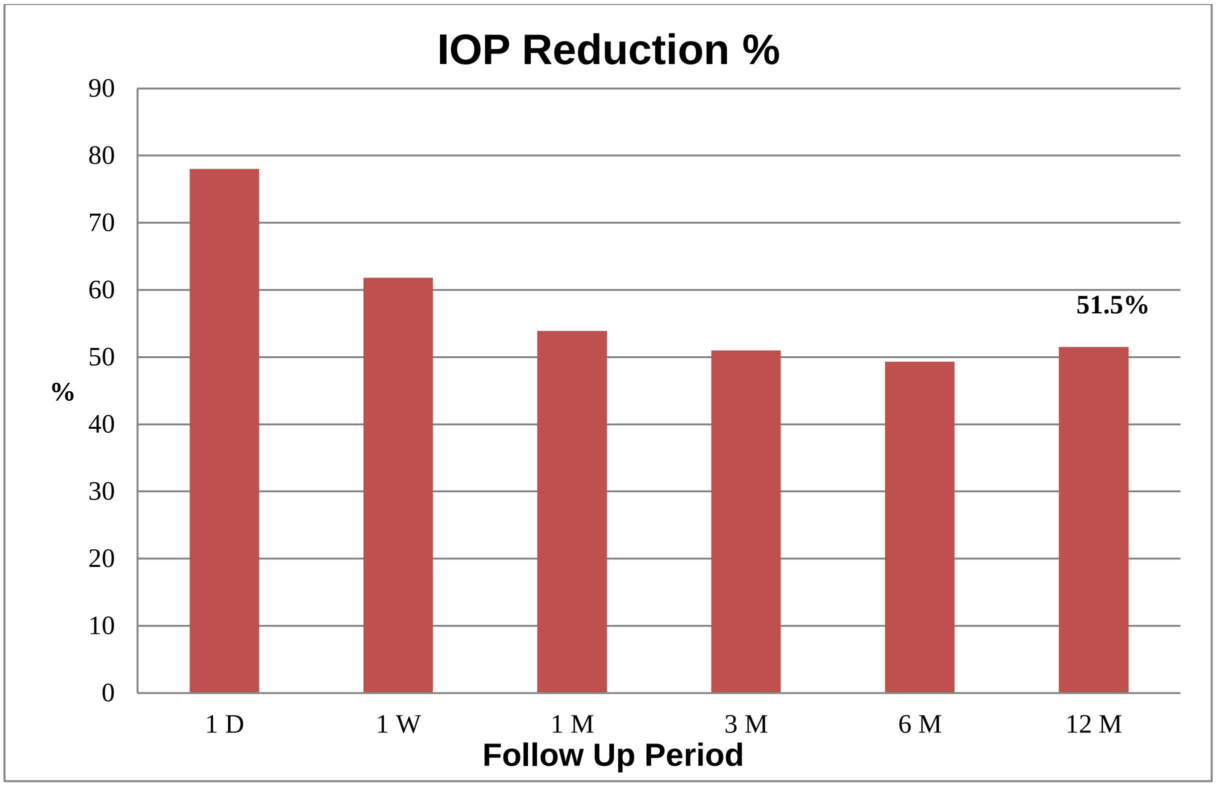

Figure 14.2: IOP reduction (%) over 12 months.

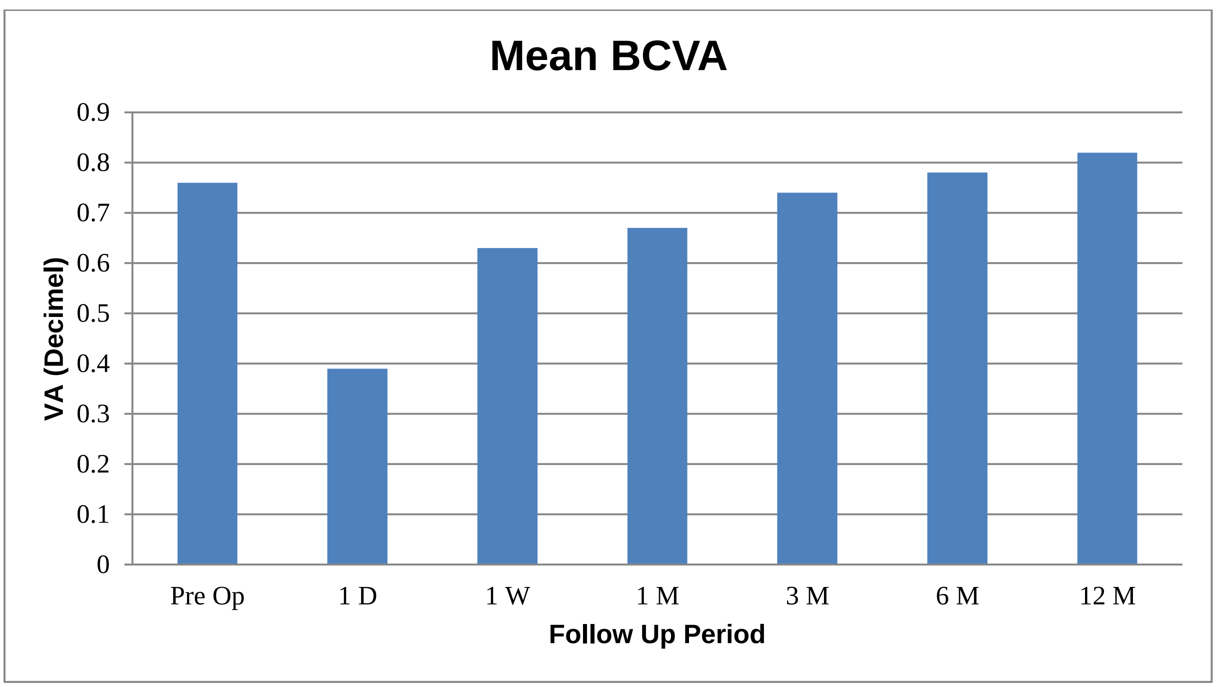

Figure 14.3: Mean BCVA over 12 month period.

Adjunctive Procedures:

Adjunctive procedures to control the IOP, as needling (with injection of anti-metabolites) or GPT were required in 16 of the 28 eyes. Of those 16 eyes, 6 required more than one procedure. The average amount of procedures needed was 2.43 ($P<0.12$). The mean IOP in those 16 eyes before the first procedure was done was 19.2 ± 3.41 mmHg. Mean duration postoperatively until first adjunctive procedure was carried out was 84.9 ± 81.2 days. In one case after GPT, incarceration of the iris into the TDM ensued; and another laser synchiolysis was done to dislodge the incarceration, and successful repositioning of the iris was achieved.

Success Rate:

At 12 months the **complete success rate was 86%** and the **qualified success rate was 96%**, respectively **(Figure 14.6).**

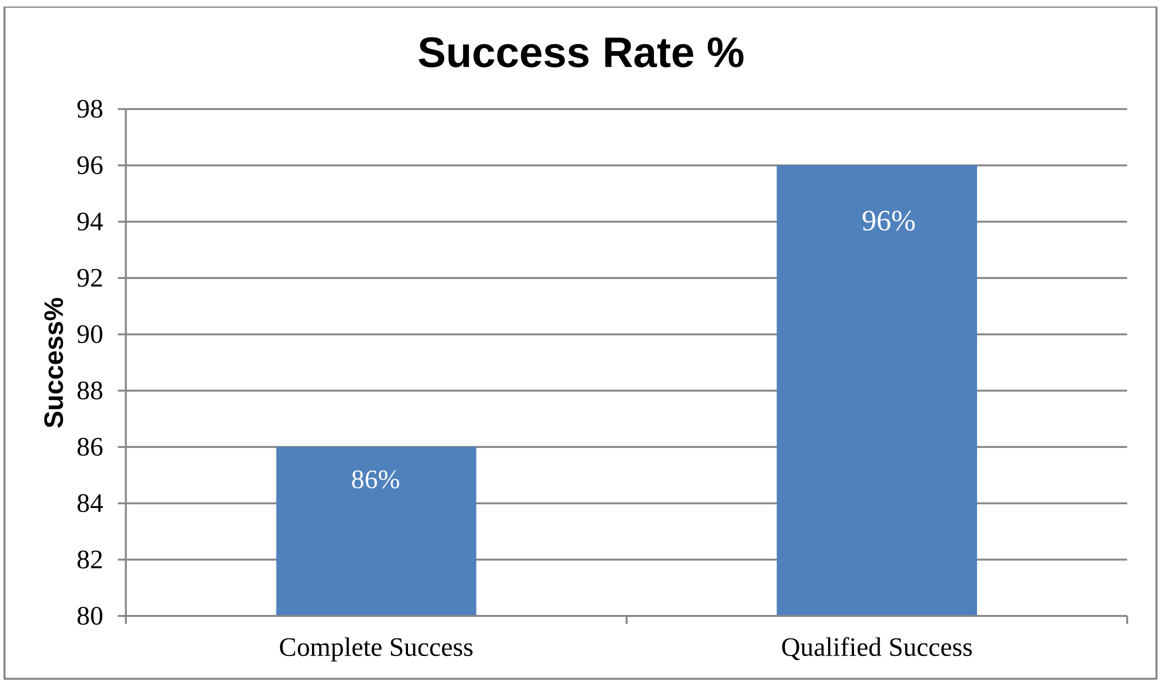

Figure 14.4: Chart showing degree of success after 12 months.

UBM ANALYSIS OF BLEB MORPHOLOGY:

UBM imaging of the blebs was performed on 9 of the 15 eyes that underwent surgery at the Clinique de Montchoisi, at 12 months. **Table 14.2** shows the patient demographics, IOP measurements and anti-glaucomatous medication intake of the 9 eyes that were imaged.

Table 14.2: Patient demographics, IOP measurements, IOP-lowering medication intake statistics, and success rates of the 9 eyes imaged with UBM.

	RESULTS
Number of Eyes Imaged	9
Mean Duration (days) of Imaging Postoperatively (Mean ± SD)	373 ± 15.5
Sex (Male %)	22% (2/9)
Age (Mean ± SD)	73.6 ± 10.0
Diagnosis No. %	POAG 56% (5/9); PEX 44% (4/9)
State of Lens No. % (Pseudophakic/Phakic)	Pseudophakic 44% (4/9); Phakic 56% (5/9)
Eye Imaged No. %	Right 5/9 (56%); Left 4/9 (44%)
Preoperative IOP (Mean ± SD)	23.7 ± 6.7 mmHg
Postoperative IOP at 12 months (Mean ± SD)	12.9 ± 3.5 mmHG
% IOP Reduction after 12 months	45.6%
Number of Preoperative Medications (Mean ± SD)	2.9 ± 1.2
Number of Postoperative Medications at 12 months (Mean ± SD)	0.2 ± 0.4
% Meds Intake Reduction after 12 months	93%
No. Requiring Adjunctive Procedures (%)	66.7% (6/9)
Complete Success %	89% (8/9)
Qualified Success %	89% (8/9)

Analysis of Outflow Facility:

Figures 14.7 to 14.11 show examples of the captured UBM images of the surgical site, taken in the longitudinal axis (90°).

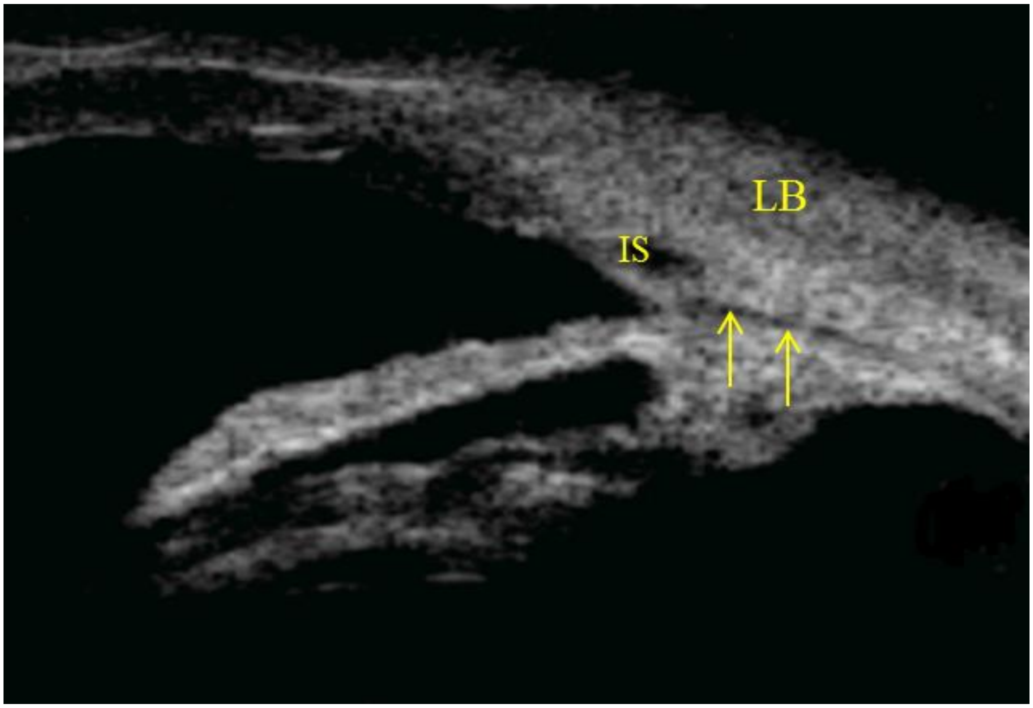

Figure 14.7: LB indicates low reflective subconjunctival bleb; IS, intrascleral (decompression) space; arrows, supraciliary hypoechoic area (suprachoroidal space).

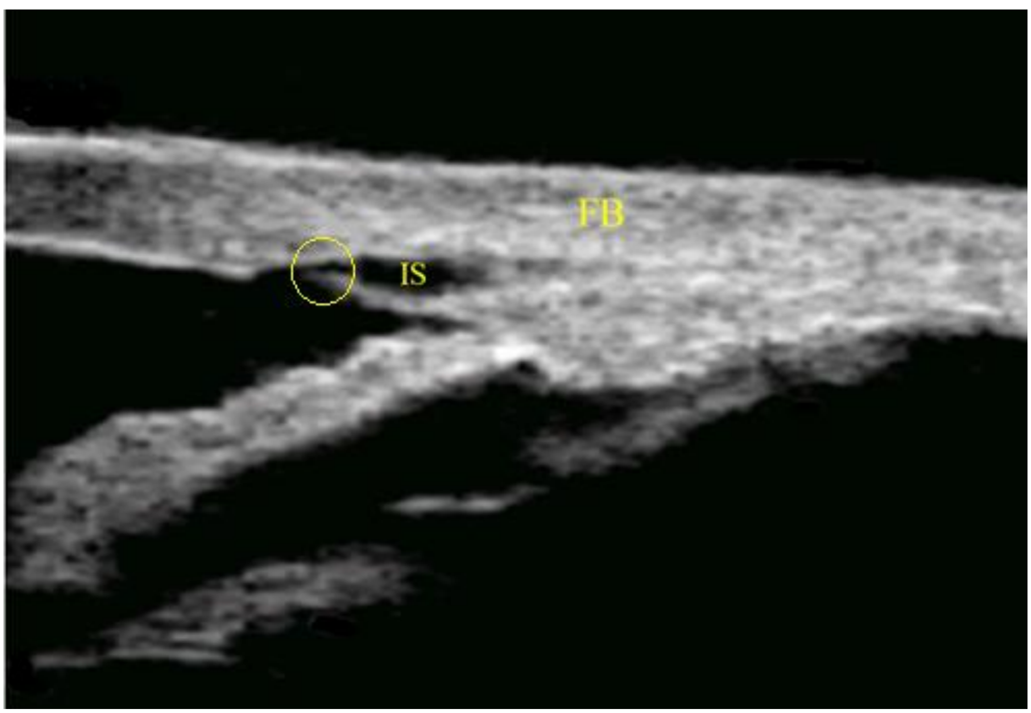

Figure 14.8: Flat subconjunctival bleb (FB), a well-established intrascleral space (IS) with an open TDM (circle), and absence of a suprachoroidal space.

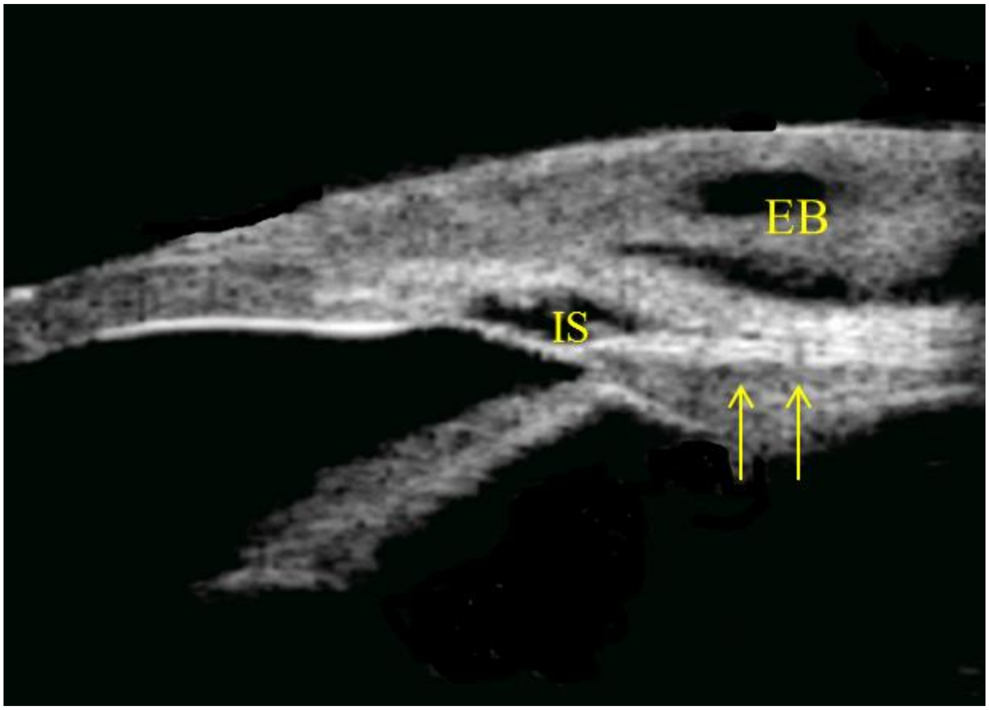

Figure 14.9: Encapsulated subconjunctival filtering bleb (EB). The intrascleral (decompression) space is well formed (IS) with a closed TDM. Arrows indicate presence of a suprachoroidal space.

Figure 14.10: Presence of a low reflective subconjunctival bleb (LB), intrascleral space (IS) with an opened TDM (circle), and a suprachoroidal space (arrows).

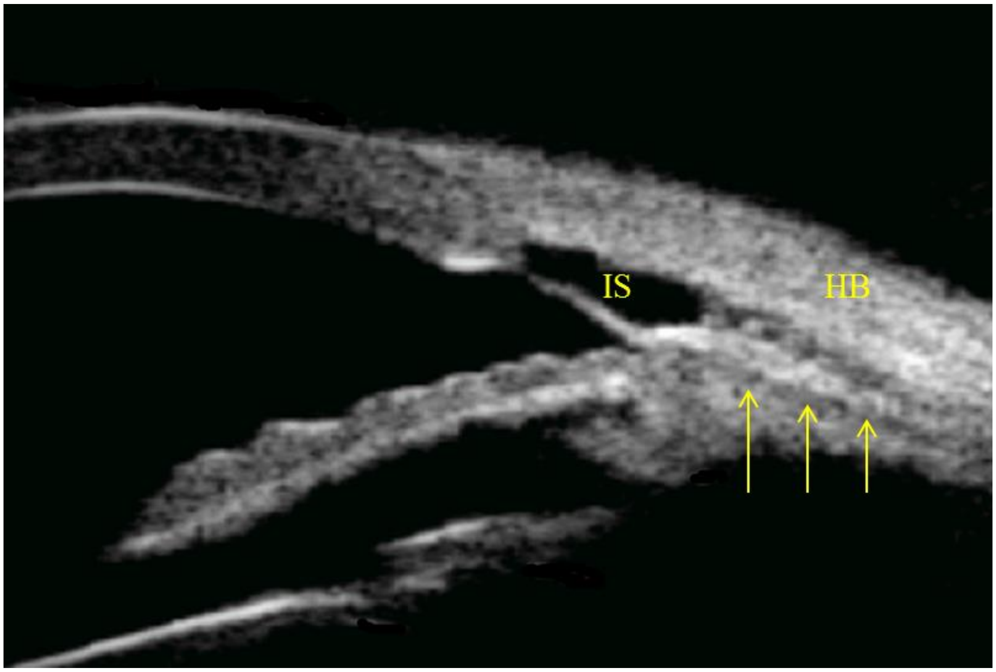

Figure 14.11: Presence of high reflective subconjunctival bleb (HB), intrascleral space (IS), and suprachoroidal space (arrows).

UBM imaging demonstrated a conjunctival bleb in the 9 patients (100%), an intrascleral (decompression) space in 8 (89%), and a supraciliary (suprachoroidal) hypoechoic area in 6 (67%). **Table 14.3** shows the frequency of each UBM feature and the types of conjunctival blebs detected. Just as with UBM, a conjunctival filtering bleb was visible with clinical slit-lamp examination in all 9 eyes.

Table 14.3: Frequency of distribution of each UBM feature in the 9 patients examined.

UBM FEATURE	EYES WITH UBM (FEATURE/TOTAL EYES)	%
Conjunctival Bleb	9/9	100
High Reflective	5/9	56
Low Reflective	2/9	22
Flat	1/9	11
Encapsulated	1/9	11
Intrascleral Space	8/9	89
Supraciliary Hypoechoic Area	6/9	67
Trabeculo-Desmectic Membrane	8/9	78
Not Perforated	6/8	75
Perforated	2/8	25
None	0/9	0

As displayed in Table 14.3, an intrascleral space and TDM could be detected in all but one eye. **Table 14.4** demonstrates the dimensions of the intrascleral space, and **Table 14.5** displays the mean thickness of the TDM measured in eight of the nine eyes (detection of TDM was not possible in one eye). Six of those nine patients had undergone GPT; however, of those six, only two had a TDM with a visible opening.

Table 14.4: Average dimensions of the intrascleral space at 12 months.

INTRASCLERAL SPACE		
DIMENSION		RESULTS (N=8)
Maximum Length (mm)	Mean	3.27
	SD	0.72
	Maximum	4.38
	Minimum	2.09
Maximum Width (mm)	Mean	1.90
	SD	0.81
	Maximum	3.20
	Minimum	0.81
Maximum Height (mm)	Mean	0.41
	SD	0.10
	Maximum	0.50
	Minimum	0.22
Volume (mm^3)	Mean	1.40
	SD	0.93
	Maximum	3.08
	Minimum	0.32

Table 14.5: Mean thickness of TDM.

TRABECULO-DESCEMET'S MEMBRANE		
DIMENSION		RESULTS (mm) (N=8)
Thickness	Mean	0.19
	SD	0.05
	Maximum	0.28
	Minimum	0.14

Six out of the nine eyes had all three features, two eyes had two features and only one eye had just one feature. In the group with 2 features, a filtering subconjunctival bleb and a decompression space were present; however, a supraciliary hypoechoic area could not be detected. **Table 14.6** displays the relationship between the distribution of UBM features detected in correlation with IOP reduction, IOP-lowering medication intake and volume of intrascleral space (IS).

Table 14.6: Relationship of distribution of UBM features in association with IOP reduction and IOP-lowering medication intake.

# UBM FEATURES (Out of 3)†	# of EYES	MEAN PREOP IOP (Mean ± SD)	MEAN POSTOP IOP (12 months)	% IOP DROP (after 12 months)	MEAN # PREOP MEDS INTAKE (Mean ± SD)	MEAN # POSTOP MEDS INTAKE at 12 months (Mean ± SD)	% MEDS INTAKE DROP (after 12 months)	MEAN VOLUME (mm^3) of IS (Mean ± SD)	MEAN THICKNESS (mm) OF TDM (Mean ± SD)	CS %	QS %
3/3	6/9	22.2 ± 7.8	11.2 ± 2.1	**49.5**	3 ± 1.5	0.2 ± 0.4	93	1.41 ± 1.09	0.20 ± 0.05	100	100
2/3*	2/9	25.0 ± 1.4	14.5 ± 0.7	**42.0**	2.5 ± 0.7	0 ± 0	100	1.34 ± 0.33	0.19 ± 0.35	100	100
1/3**	1/9	30.0 ± NA	23.0 ± NA	**33.3**	3.0 ± NA	1.0 ± NA	66.7	0	0	0	0

†Those 3 features are subconjunctival filtering bleb, IS and presence of a supraciliary hypoechoic area.
*Subconjunctival bleb and IS detected; no supraciliary hypoechoic area
**Only subconjunctival bleb detected; no IS, TDM or supraciliary hypoechoic area.
IS = Intrascleral (decompression) Space
CS = Complete Success (≤21 mmHg without meds, with or without adjunctive procedures)
QS = Qualified Success (≤21 mmHg with meds, with or without adjunctive procedures)

There was no statistically significant correlation between the volume of the intrascleral space and the level of IOP (r=-0.7696, *P* = 0.02) **(Figure 14.12)**. However, there was a significant correlation between the thickness of the TDM (r=0.3187, *P* = 0.05) and IOP. In the 6 patients with presence of all 3 UBM findings simultaneously, the target IOP success rate was 89%. This target was not achieved in the patients with 1 or 2 findings. In the 2 patients with 2 UBM features, subconjunctival bleb and intrascleral space were detected, however a hypoechoic area in the suprachoroidal space was not. Therefore, the difference between the group with 3 and 2 findings was presence of a supraciliary hypoechoic area. In single patient with only one UBM feature (subconjunctival bleb); none of the success targets were achieved. Therefore, lower IOP levels were achieved when of all 3 features were present.

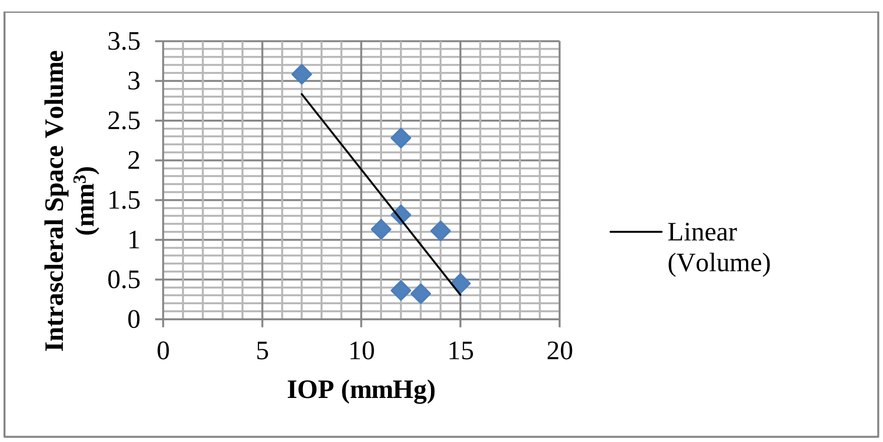

Figure 14.12: Correlation between intrascleral space volume and IOP level.

15. DISCUSSION:

Deep sclerectomy with implantation of a space-maintaining device in the suprachoroidal space is a relatively novel technique, even though the concept of decreasing IOP by directing aqueous humor into this area is not.[14] Multiple studies have been published regarding DS with intrascleral space-maintaining implants,[85,120-123] however, only 1 clinical trial has been published in relation to DS alone with the use of implants in the suprachoroidal region. Mućoz[13] analyzed the efficacy of DS with the use of a T-Flux implant, with the body of the device placed in the suprachoroidal space and the arms into Schlemm's canal. At one year, he demonstrated a complete success rate (IOP <22mm Hg without medication) of 73.8%, and a qualified success rate (IOP <22mm Hg with or without medication) of 93.4%.

In this study, complete success rate at 1 year was 86%, the qualified success rate was 96%, with a mean IOP of 11.7 ± 2.6 mmHg, generating average IOP reductions of 51.4%. Preoperative use of ocular anti-glaucomatous medications decreased from a mean of 2.57 ± 1.07 to 0.18 ± 0.39 at 12 months postoperatively. The surgical success rates and medium-term IOP results in this study are similar with those reported to date for DS performed with an intrascleral collagen implant,[85,120-123] and to the study conducted by Mućoz.[13]

In our clinical trial, the rate of postoperative complications was minimal; correlating with the rate demonstrated in the published studies of deep sclerectomy, either alone,[41-43,45-47,85,115-124] or in comparison to trabeculectomy.[141,142] In trabeculectomy, there is a less controlled filtering mechanism due to the direct communication between the anterior chamber and the space beneath the conjunctiva.[141] In DS, the TDM allows better regulation of aqueous humor elimination, decreasing the incidence of postoperative complications as hypotony and hyphema.[143] In our study, one eye suffered from hyphema (3.6%), and another case from ciliary body (CB) detachment (3.6%) due to severe hypotony. There was a single incidence of iris incarceration into the TDM, however, this occurred post-GPT, and not as a result of the surgery. Insertion of the collagen implant into the suprachoroidal space by the 2 experienced surgeons that performed the surgeries was described as being simple and straight forward, requiring less effort and maneuvers than implantation into the decompression space. No complications related to the incorporation of the collagen implant into the suprachoroidal space were reported.

DS may lead to a diminution of IOP through variable mechanisms. These include the establishing of a conjunctival filtering bleb; eradication of tissue at the site of greatest resistance of flow, the juxtacanalicular meshwork; suprachoroidal filtration; and via the absorption through the intrascleral space. [63,103]

UBM can be utilized to examine bleb morphology and tissue changes after glaucoma surgery. It gives information that slit-lamp examination cannot provide. It allows the internal visualization of the surgical site and the measurement of the dimensions of the intrascleral space and thickness of TDM.[135] One of the goals of this clinical trial was to analyze aqueous outflow pathways by studying the correlation of IOP control with the morphology of four features, three of them aqueous outflow routes. Those three aqueous elimination signs are the subconjunctival filtering bleb, intrascleral space and supraciliary hypoechoic area. The fourth morphological feature examined was the TDM.

In this study, only nine eyes included in the trial underwent UBM imaging for analysis of bleb morphology and outflow facility. Even though this is a small fraction of the total number of eyes involved in the clinical trial, other studies[21,40,134,140] have included similar numbers.

In our study, the detection of a TDM and intrascleral cavity was a typical finding. Marchini et al[11] in a study on UBM after deep sclerectomy with reticulated hyaluronic acid implants, reported a correlation between the presence of three characteristics with IOP reduction outcome; the reflectivity of the conjunctival bleb, the intrascleral cavity; and the suprachoroidal (supraciliary) hypoechoic area. In our study, the simultaneous existence of an intrascleral space, a subconjunctival bleb and a supraciliary hypoechoic area was associated with IOP reduction and surgical success.

In our study, the existence of an intrascleral cavity was a typical finding, present in 89% of cases. This could be due to the implantation of only one-half to two-thirds of the collagen implant in the suprachoroidal space, providing space maintenance in both the suprachoroidal area and the intrascleral cavity. In agreement with previous reports,[86,138,140] and in disagreement with a study done by Mavrakanas et al[36], the intrascleral cavity volume did not appear to be correlated with IOP regulation (r=-0.7696, P = 0.02).

There are two studies in literature analyzing the correlation between the thickness of TDM and IOP levels. Aptel et al[134] stated that lower IOP correlated with TDM thickness (P = 0.01); and Cabrejas et al[139] described that a thinner TDM was significantly correlated with lower postoperative IOP value at the first postoperative month (r=0.45, p=0.05). In this study, six of the eight TDMs that were detected were not perforated, even though four of those six had previous goniopuncture i.e. only two of the eight were never perforated. From the statistical analysis of those two patients, we found a significant correlation between the thickness of the TDM and IOP level (r=0.3187, P = 0.05), similar to previous reports.

Regarding the suprachoroidal hyporeflective area, previous studies have shown conflicting reports. Chiou et al[21] concluded that its existence correlated with reduced IOP levels. Roters et al[140] detected this hypoechoic region in six of nine patients 12 months post-viscocanalostomy, but stated that its presence did not correlate with IOP reduction. Negri–Aranguren[86], in another study regarding viscocanalostomy, concluded that this feature was detected in just two of 23 eyes and could not be considered a prominent pathway for aqueous elimination. Marchini et al[11] detected this finding in 60% of cases 12 months after DSCI. Kazakova et al[135] reported a strong association between IOP regulation and outflow thought the suprachoroidal region in DSCI. In this study, the results were similar to the findings of Kazakova et al, and a suprachoroidal hyporeflective area was found in 67% of cases after 12 months postoperatively. A significant correlation was found between suprachoroidal aqueous outflow and IOP control ($P = 0.05$).

Different degrees of reflectivity of subconjunctival blebs have routinely been found after trabeculectomy.[136] However, Negri-Aranguren et al[86] 7-9 months post-viscocanalostomy detected only one filtering bleb. Kazakova et al[135] documented the existence of a clinically diffuse filtering bleb in 40 out of 43 eyes, with a subconjunctival space in all of them. They considered the presence of this sign an indication of continuous filtration after DCSI, at long-term follow-up. In our clinical trial, subconjunctival filtering blebs were found in 90.9% of cases, with the high reflective type being the most common (50%). The presence and type of filtering bleb were not associated with the surgical end result; as qualified surgical success was achieved in one patient without a filtering bleb, and in another with an encapsulated bleb. Roters et al[140] reported that two eyes with a subconjunctival filtering bleb of the low-reflective type required extra surgery, and proposed that even a diffuse low-reflective filtering bleb, 30 days post-viscocanalostomy, was not an indication of solid IOP regulation.

The suprachoroidal space possesses certain anatomical and physiological that render it an appealing and useful route; resulting in safer techniques with improved surgical success, leading to an increase in patients' quality of life.[144] According to numerous studies,[56-61] implantation of suprachoroidal devices appears to be a straight forward procedure with a reasonable learning curve. The advantages of these implants arise from the fact that there is 'no bleb'. This permits the avoidance of the adverse events that accompany subconjunctival filtration blebs; which include leakage, hypotony, bleb failure, bleb-related infection, and discomfort with foreign body sensation or pain.[146] The ab-interno implantation methods also allow the preservation of the structural integrity of the conjunctiva, by sparing it and by reducing infection. This seems to be confirmed by the overall positive results found for most devices in terms of safety and adverse events.[56-61] However, the results of the clinical studies published so far indicate that IOP reduction obtained by devices are still inferior to standard trabeculectomy. [144]

In our study, suprachoroidal flow apparently plays a role in the mid-term reduction of IOP; nonetheless, the long-term effect still needs to be elucidated. The short follow-up period (12 months) and the absence of a control group in this study certainly pose considerable challenges. There are conflicting reports regarding the importance of the suprachoroidal space in NPGS and its role in aqueous outflow, therefore many questions still need to be answered. The possibility of this space remaining patent after longer periods still needs to be evaluated. The uvea is a highly muscular region with myofibrils,[28] and the ability of space-maintaining implants to have a long-term limiting effect on the action of fibrosis in this space is another area that needs to be explored. Laser goniopuncture can be performed to correct subconjunctival bleb failure,[145] however, no equivalent procedure exists for suprachoroidal implant failure.

In conclusion, DS with suprachoroidal collagen implant appears to be a safe and effective surgical procedure for the reduction of IOP; however, long term studies are still required to confirm this finding.

16. RÉSUME FRANÇAIS:

INTRODUCTION:

Les définitions du glaucome ont beaucoup évoluées durant le siècle passé, et ce jusqu'à ce jour, elles restent imprécises et sous réserve d'ajustements. Actuellement, le terme relève d'un groupe de pathologies, plutôt que d'une seule entité, de physiopathologie, présentation clinique et gestions différentes.

Le glaucome est un ensemble de neuropathies qui affectent le disque optique, sous forme d'une excavation pathologique caracteristique. Cette neuropathie optique est caractérisée par des deficits dans la couche des fibres nerveuses, associés à des anomalies correspondantes du champ visuel. Le glaucome est souvent, mais pas toujours, associé à des niveaux élevés de pression intra-oculaire (PIO).

Le traitement du glaucome repose sur trois protocoles: le traitement médical, le traitement au laser et/ou la chirurgie. La trabéculectomie a toujours été considérée comme la méthode chirurgicale la plus efficace et la plus reproductible pour la réduction du taux de la PIO. Sa capacité à réduire la PIO à des niveaux suffisants, permettant la protection du nerf optique et la rétine de toute atteinte l'a rendue une réference comparable aux autres techniques chirurgicales filtrantes. Par ailleurs, ses complications sont nombreuses; y compris l'hypotonie, l'induction de la cataracte ou l'activation de sa progression, l'effusion de la choroide, l'hyphéma, la mauvaise cicatrisation de la bulle de filtration, et l'endophtalmie liée à la bulle.

La chirurgie filtrante non-pénétrante du glaucome (CNPG) a été créée comme une méthode alternative à la trabéculectomie, en raison d'une efficacité similaire dans la réduction de la PIO, avec moins de complications postopératoires. Bien que de nombreuses techniques de CNPG ont été décrites, CNPG se réfère généralement à la sclérectomie profonde (SP), viscocanalostomie (VC) et canaloplastie.

SP est une procédure de filtrage qui permet l'écoulement de l'humeur aqueuse de la chambre antérieure vers l'espace sous-conjonctival à travers la membrane trabéculo-descémétique (MTD), une membrane d'existence physiologique. La MTD empêche l'hypotonie postopératoire en fonctionnant comme un site de résistance à l'écoulement. D'autres avantages de SP sont les inductions minimes de changements dans l'état de réfraction de la cornée, une faible incidence d'inflammation dans la chambre antérieure (CA) en postopératoire et le faible taux de formation de la cataracte comparativement à la trabéculectomie. Egalement, les résultats de la SP ont été satisfaisants dans le glaucome à angle ouvert primitif et secondaire, une efficacité qui reste douteuse en présence d'un angle fermé ou neovascularisé.

Dans la SP, un volet scléral ressemblant à un volet de trabéculectomie est d'abord créé. Plus profondément au volet superficiel, le chirurgien dissèque une partie plus profonde de la sclérotique, révélant la MTD créée chirurgicalement. Après le passage de l'humeur aqueuse à travers la MTD, quatre mécanismes possibles de l'écoulement aqueux et d'absorption peuvent avoir lieu; à travers une bulle de filtration sous-conjonctivale, une bulle de filtration intra-sclérale (également appelé l'espace intra-scléral, l'espace de décompression ou le lac sclérale), par voie supraciliaire (suprachoroïdienne), filtration et drainage de la veine épisclérale via le canal de Schlemm.

La fibrose secondaire de la bulle de filtration intra-sclérale, est un problème commun dans la SP, et peut conduire à une insuffisance de réduction de la PIO. Pour augmenter les effets de filtration de la sclérectomie profonde, Kozlov et al proposa la mise en place d'un implant de collagène dans le lit scléral. Le concept de ce dispositif de collagène était de combler l'espace intra-scléral sous le volet superficiel au cours de la période post-opératoire précoce lorsque le processus de guérison est à son maximum. L'implant de collagène va ensuite se résorber, laissant une cavité vide à travers laquelle l'humeur aqueuse est évacuée et ensuite absorbée; agissant donc comme un dispositif de maintien de l'espace. Ces dispositifs de maintien de l'espace peuvent également être placés sous l'espace intra-scléral dans l'espace supra-choroïdien sous-jacent.

L'imagerie du segment antérieur, comme la biomicroscopie ultrasonore (UBM), permet des mesures précises du segment antérieur. Elle permet la visualisation et l'évaluation des structures qui ne peuvent pas être vus ou évalués par examen à la lampe à fente. Récemment, l'UBM a été utilisée pour analyser la morphologie de la bulle après la chirurgie du glaucome.

BUT DE L'ÉTUDE:

Cette étude est divisée en deux parties: (i) une évaluation prospective, non randomisée, contrôlée, multicentrique concernant la sécurité et l'efficacité de la sclérectomie profonde avec mise en place de l'implant suprachoroidal de collagène (ii) une étude prospective, non randomisée, monocentrique, contrôlée, pour l'évaluation de la morphologie de la bulle de filtration après un an de la chirurgie.

Les principaux objectifs de cette étude sont les suivants:

1) Etudier l'innocuité et l'efficacité de cette procédure.
2) Evaluer la morphologie des bulles de filtration après un an par imagerie UBM.
3) Analyser si l'insertion de l'implant de collagène dans l'espace suprachoroïdien conduit à la formation d'une bulle perceptible dans cette région.
4) Evaluer le rôle du flux suprachoroïdien dans SP.

TECHNIQUES DE LA CHIRURGIE NON-PÉNÉTRANTE DU GLAUCOME:

1. La sclérectomie profonde:

Un volet superficiel de la sclérotique, environ 30% de l'épaisseur sclérale, est créé avec des dimensions de l'ordre de 5×5mm à l'aide d'une lame numéro 11. Pour exposer la membrane trabéculo-descémétique (MTD), la dissection du volet scléral superficiel doit être avancée 1-1.5 mm dans la cornée en avant. Dans les cas réfractaires, une éponge imbibée de la mitomycine C (MMC) 0.28mg/ml peut être appliquée pendant 1-3 minutes sur la surface de la sclère et sous la conjonctive, avant ou après dissection du volet superficiel.

La dissection du volet scléral profond (d'où le nom de sclérectomie profonde) est réalisée à l'aide d'un couteau crescent en forme de croissant en disséquant plus profondément 4 × 4 mm dans le lit du volet précédemment disséqué, un volet profond qui par définition est de plus petite taille par rapport au volet superficiel **(figure 5.1)**.

L'incision initiale doit être suffisamment profonde jusqu'à ce que la choroïde soit exposée. Avec l'utilisation d'un couteau crescent, en avant permet de procéder à la dissection du canal de Schlemm. Le canal de Schlemm est situé en avant de l'éperon scléral, tout comme les fibres de la sclérotique commencer à avoir une orientation parallèle au limbe régulier **(figure 5.2)**.

La dissection se poursuit en avant après le pelage du canal de Schlemm afin d'avoir une grande MTD permettant de réaliser une goniopuncture au Nd:YAG, si nécessaire plus tard, et en diminuant le risque d'incarcération d'iris si la goniopuncture est faite près de l'iris (au cas où la MTD n'était pas assez grande). Afin de ne pas la perforer lors de cette étape, le stroma cornéen et la membrane de descemet (MD) sont délicatement séparés en appliquant une pression à la fin de la dissection sur le lit scléral à l'aide d'un instrument contendant ou une éponge. La dissection est prolongée en avant en effectuant la coupe radialement avec une lame numero 11, en prenant soin de ne pas toucher la MTD **(figure 5.3).**

Une fois la séparation entre le stroma et la MD est réalisée, l'excision du volet profond est complétée à l'aide de ciseaux émoussés **(figure 5.4).** En utilisant une petite pince émoussée, le canal de Schlemm dans sa paroie intérieure et le trabéculum adjacent sont détachés; ils apparaissent comme une membrane élastique mince juste en avant de l'éperon scléral **(figure 5.5).** La suppression de ces structures est appelée trabeculectomie ab-externo. A fin de maintenir l'espace créé dans le volet de la sclérotique, l'implantation d'un dispositif occupant peut être fait **(figure 5.6).**

L'utilisation d'implants dans la sclérectomie profonde:

La fibrose secondaire des bulles de filtration dans la SP est un obstacle majeur à l'obtention de succès à long terme et au contrôle ultérieur de la PIO. Pour aborder cette question, Kozlov et al décrit l'utilisation d'un implant de collagène placé dans le lit scléral. Le concept de l'implant de collagène était de combler l'espace intrascléral sous le volet superficiel pendant la période postopératoire précoce où le processus de guérison est à son maximum. L'implant de collagène est ensuite résorbé, laissant une cavité vide à laquelle l'humeur aqueuse est filtrée puis absorbée.

D'autres implants, de la même fonction et de conception différente, ont également été proposés; et tout récemment, les implants ont été placés sous le lit scléral dans l'espace suprachoroïdien sous-jacent **(figures 5.7 et 5.8).**

2. La viscocanalostomie:

Cette opération a été décrite par Stegmann. Des volets scléraux triangulaires ou carrés superficiels et profonds sont façonnés (similaire à sclérectomie profonde), la création d'un orifice dans le canal de Schlemm. Le hyaluronate de sodium de haute viscosité est injecté dans le canal de Schlemm pour améliorer le drainage de l'humeur aqueuse par cette voie **(figure 5.16).** Le concept derrière cette procédure est de tenter de regagner l'écoulement naturel de l'humeur aqueuse sans formation d'une bulle de filtration.

3. La canaloplastie:

Canaloplastie est une intervention non pénétrante réalisée en utilisant la totalité de la circonférence du canal de Schlemm sans effectuer une fistule ou créer une bulle. L'opération est une modification de la viscocanalostomie; après que le canal est exposé, elle est pourvue d'une canule sur toute sa circonférence avec injection d'un matériel viscoélastique suffisant pour provoquer une dilatation du canal. Une fois que le canal de Schlemm de pleine longueur est traversé par la canule, un fil de suture 10/0 est attaché à son extrémité et la canule est retirée, le fil de suture est placé dans la lumiere du canal. La suture est ensuite attachée pour assurer une tension suffisante pour le canal et laissée en place **(figure 5.17).**

4. La sclérectomie assistée par laser CO_2 (CLASS):

Dans CNPG, la dissection du volet scléral profond est la partie la plus difficile, qui nécessite une expérience et une précision. Lors de la dissection manuelle avec une lame, la perforation accidentelle de la MTD mince est une complication fréquente qui se produit chez près de 30% des patients au début de la phase d'apprentissage de cette procédure et à un taux de 3% chez le chirurgien expérimenté.

Irradiation du laser de CO2, en raison de ses caractéristiques uniques, a été suggérée par Assia et al comme un moyen moins difficile de faire la sclérectomie profonde. Après, le volet superficiel est façonné, des applications répétées de laser CO2 conduit à l'ablation progressive du tissu scléral profond jusqu'à cet écoulement de l'humeur aqueuse **(Figure 5.18).** La liquide écoulé absorbe l'energie du laser, ce qui permet d'arreter progressivement l'ablation, ceci est un moyen de prévention, contre la perforation du tissu scleral mince restant.

MÉCANISMES DE FILTRATION DU CNPG:

Dans le glaucome à angle ouvert primitif, le site principal de la résistance de l'écoulement aqueux sont les mailles juxtacanaliculaires et la paroi interne du canal de Schlemm. En supprimant ces structures chez les patients atteints de glaucome à angle ouvert, la facilité d'écoulement peut être améliorée. La MTD jouera le rôle d'un site de résistance à l'écoulement aqueux, empêchant la diminution soudaine de la PIO et en évitant par conséquent l'hypotonie postopératoire et ses complications. Rossier et al ont démontré que la diminution de la PIO était 5.5 fois plus rapide après trabéculectomie ab-externo qu'après SP seule. Après son passage dans la MTD l'humeur aqueuse peut se résorber par quatre mécanismes : filtration de vésicules intra-sclérales, une bulle de filtration sous-conjonctivale **(figure 7.1)**, une filtration suprachoroïdienne, et à travers le canal de Schlemm vers la veine episclérale.

INDICATIONS, CONTRE-INDICATIONS ET COMPLICATIONS DE LA CNPG:

Indications:

1) **Glaucome à angle ouvert primaire et secondaire.**
2) **Glaucome uvéitique.**

3) **Le glaucome juvénile et le glaucome congénital.**
4) **Le glaucome dans le syndrome de Sturge Weber.**
5) **Les myopies fortes.**

Contre-indications:

L'angle étroit est considéré comme une contre-indication relative, comme dans ces cas CNPG peut être compliquée avec l'incarcération de l'iris ou de synéchie antérieure. Il est absolument contre indiqué d'effectuer les CNPG dans le glaucome néovasculaire.

Complications:

CNPG sont connus pour avoir moins de complications en comparaison avec la trabéculectomie. L'écoulement lent de l'humeur aqueuse par la MTD empêche la réduction soudaine de la PIO empêchant ainsi une hypotonie soudaine. Aussi l'acuité visuelle est en général non altérée et retrouve ses niveaux préopératoires autour de la première semaine post-opératoire. Ceci est principalement dû à de faibles niveaux d'inflammation après la chirurgie car aucune iridectomie périphérique n'est effectuée. Quelques cas de CNPG sont associés à des complications spécifiques qui pourraient être peropératoires, postopératoires précoces ou tardives.

1. Complications peropératoires:

MTD perforation est la complication peropératoire la plus vue des CNPG au cours de la phase d'apprentissage. Une perforation dans 30% des cas a été signalée, ce pourcentage diminue avec l'expérience chirurgicale accrue, pour devenir de 3.1%.

2. Les premières complications postopératoires:

a) **Bulles de filtrations et seidel:** test de Seidel positif ou fuites sont souvent dues à la fermeture inadéquate de la conjonctive. Fuite s'arrête généralement spontanément après quelques jours.
b) **Hypotonie et de ses complications:** l'hypotonie précoce peut survenir chez certains patients pour quelques jours mais habituellement avec une chambre antérieure bien formée. Il est considéré comme un indicateur positif pour le contrôle de la PIO sur le long terme. La persistance de l'hypotonie n'est pas commune, mais si c'est le cas, la maculopathie hypotonique peut survenir, similaire à celle retrouvée dans la trabéculectomie.
c) **L'inflammation.**
d) **Détachement de la membrane de Descemet (figure 10.1).**
e) **Blebitis:** est une condition potentiellement aveuglante **(figure 10.2)** qui peut se produire à la fois dans la sclérectomie profonde et la trabéculectomie; et cette condition pourrait conduire à une endophtalmie.
f) **Kératite infectieuse.**
g) **La montée post-opératoire précoce de la PIO.**

3. Complications postopératoires tardives:

a) **Fibrose de la bulle:** fibrose conjonctivale conduit à la perte de la bulle. PIO élevée, l'injection conjonctivale diffuse, et la présence de grands vaisseaux tortueux sont des signes de début de fibrose. Dans le cas d'augmentation de la PIO, la gestion se compose de GPT et/ou d'une procédure de needling combinée à des injections sous-conjonctivales d'un antimétabolite.

b) **Le prolapsus synechiant de l'iris** : cette condition pourrait arriver suivant une micro perforation de la MTD ou de l'iris peropératoire, une incarcération dans des trous de la MTD aprés goniopuncture au laser YAG **(figure 10.3).** Il pourrait également se produire suite à un frottement des yeux, un traumatisme contendant, ou quand le patient tousse, conduisant à la rupture de la MTD, résultant d'un prolapsus de l'iris. Une synechiolyse au laser et le traitement médical pourraient être tenté afin de repositionner l'iris. En cas d'échec une intervention chirurgicale pourrait être nécessaire notamment en cas de PIO élevée.

c) **L'astigmatisme cornéen et la perte de cellules endothéliales:** la réfraction postopératoire et l'acuité visuelle pourraient être affectés par la courbure de la cornée modifié chirurgicalement.

d) **L'ectasie sclérale.**

BIOMICROSCOPIE ULTRASONORE (UBM):

UBM a récemment été utilisée pour évaluer les bulles de filtration après la chirurgie du glaucome. Elle permet la visualisation de la zone post-opératoire; permettant la mesure de l'épaisseur de la MTD, les dimensions de l'espace intra-scléral, la présence ou l'absence d'un espace suprachoroïdien et de la morphologie de la bulle sous-conjonctivale **(figure 12.1)**. Elle permet également la visualisation des altérations structurelles causées par la filtration post-chirurgie, en aidant à la compréhension de son mécanisme d'action et les causes anatomiques de l'échec de la chirurgie.

MATÉRIAL ET MÉTHODE:

Cette étude est divisée en deux parties: (i) une évaluation prospective, non randomisée, controlée, multicentrique concernant la sécurité et l'efficacité de la sclérectomie profonde avec mise en place de l'implant suprachoroidal de collagene (ii) une étude propective, non randomisée, monocentrique, controlée, pour l'évaluation de la morphologie de la bulle de filtration aprés un an de la chirurgie. Elle a été réalisée en Suisse, conformément à la Déclaration d'Helsinki. Un document de consentement éclairé a été signé par tous les patients avant le début de l'étude. Les essais cliniques ont été effectués dans le secteur de glaucome à l'hôpital de l'Université de Genève, et dans le département Glaucome à la Clinique de Montchoisi à Lausanne.

28 cas on été inclus dans cette thèse, 15 ont été réalisés à la Clinique de Montchoisi et 13 à l'université de Genève (HUG). Tous les cas de la Clinique de Montchoisi ont été operés par un seul chirurgien, Professeur André Mermoud (AM) et ceux faits à l'HUG, fut operés par Dr.

Tarek Shaarawy (TS). Les deux chirurgiens ont collaborés pour suivre le meme protocol chirurgical, utilisation du meme dispositif de collagène, et la meme technique d'implantation. 9 des 15 patients operés à la Clinique de Montchoisi, ont béneficié d'une imagerie par UBM en post-operatoire pendant une durée de 12 mois. L'UBM a été réalisée uniquement chez les patients operés à la Clinique de Montchoisi, ceci est du au fait que chaque centre à une machine UBM différente, ainsi pour uniformiser la méthode d'imagerie et éviter toutes les divergences qui pourraient compromettre le protocol de l'étude, les collaborateurs ont décidé d'utiliser une seule machine. Les collaborateurs n'ont pas estimé compromettant l'implication de deux chirurgiens différents dans le protocol de l'étude. C'est pourquoi l'étude divisé en deux parties. Mon role (le candidat au doctorat) dans cette étude était d'examiner et de suivre les patients durant la phase pré et post-opératoire, avec la réalisation et l'analyse de l'imagerie par UBM.

Tous les patients ont été complètement examinés à la fois en préopératoire et postopératoire. Toutes les complications peropératoires ont été documentées et postopératoires également des examens de suivi ont été réalisés dès le premier jour après l'opération, à une semaine, un mois, et 3, 6 et 12 mois. Un examen à la lampe à fente examen du segment antérieur, de mesure de la PIO et un fond d'œil ont été effectués à chaque visite. UBM imagerie du segment anterieur et de filtrage de la bulle a été fait une fois à 12 mois. Toutes les procédures effectuées comme adjuvantes goniopuncture et needling ont été notées, avec mesure de la PIO avant et après la procédure enregistrée. Tout médicament anti-glaucomateux adjuvant utilisé a également été documenté.

Technique chirurgicale:

Toutes les opérations ont été réalisées par deux chirurgiens expérimentés en utilisant un microscope opératoire. La conjonctive a été ouverte au limbe. A 5 × 5 mm volet scléral superficiel a été disséqué à une profondeur d'un tiers d'épaisseur sclérale, articulé en arrière. Ce volet scléral superficiel a été étendu 1-1.5 mm en avant dans la cornée claire. L'incision initiale a été faite avec une lame numero 11, et la dissection horizontale avec un couteau crescent de microchirurgie. Les éponges imbibées de mitomycine 0.02% ont été placés pendant 2 minutes dans le lit scléral et entre la sclère et la capsule de Tenon, et ces sites ont ensuite été irrigués avec une solution saline équilibrée. Une sclerokeratectomie profonde a été réalisée en disséquant un second volet scléral profond 4 × 4 mm de base à l'extrémité antérieure du lambeau superficiel avec deux incisions latérales et une postérieure profonde incision scléral faite avec une lame de diamant. Le volet scléral profond a ensuite été disséqué en avant avec la lame au toit du Schlemm canal et un autre 1-1.5 mm plus en avant pour enlever le tissu sclérocornéen sur le trabéculum antérieure et la ligne Schwalbe, et la création de la MTD mince **(figure 13.1).** Le volet scléral profond a ensuite été retiré avec des ciseaux **(figure 5.3).**

A ce stade, la filtration d'une solution aqueuse à travers le trabéculum a été observée. Le trabéculum justacanaliculaire et l'endothélium du canal de Schlemm ont ensuite été éliminés en utilisant une pince fine lisses **(figure 5.5).** Une incision horizontale de 1.5-2 mm est faite dans le lit scléral profond restant, environ 1mm postérieure à l'éperon scléral, créant une poche sous-scléral **(figure 13.2).** Un implant de collagène [Aquaflow, STAAR (Surgical AG Nidau, Suisse) **(figure 5.9)**] a été ensuite placé dans cette poche dans l'espace suprachoroïdien sous-jacent. Environ la moitié aux deux tiers de l'implant est placée dans cette poche, la partie restante dans la cavité intra-scléral **(figure 13.3).** Le volet scléral superficiel est ensuite suturé vers le bas avec un fil de nylon 10/0, puis la conjonctive avec sutures vicryl 8/0 **(figure13.4).**

UBM procedure d'imagerie at d'analyse:

Dispositif UBM:

Modèle BHF-50 Lin (Aviso, Quantel Medical, France) avec un transducteur de 50 MHz a été utilisé.

Procédure:

Les patients ont été placés dans la position assise. Des gouttes anesthésiques topiques ont été instillées dans l'œil examiné. Un seul opérateur effectue les procédures d'imagerie pour tous les yeux étudiés. L'instrumenta été fixé à100dB de gain. La zone de sclérectomie à 12 heures a été explorée à la fois selon l'axe longitudinal (radial ou antéro-postérieur) et transversal (parallèlement au limbe) scans. Des mouvements de la sonde ont été réalisés pour explorer les structures concernées dans une direction perpendiculaire.

Analyse:

Les facteurs suivants ont été évalués:

- Présence de bulle de filtration sous-conjonctivale. Les bulles de filtration sous-conjonctivales ont été classés en 4 types: faible réflexion **(figure14.7)**, haute réflectivité **(figure14.11)**, encapsulées **(figure 14.9)**, et aplaties **(figure 14.8).**
- Présence et dimensions d'un espace intrascléral sous le volet scléral.
- Epaisseur de la membrane trabeculocornéenne résiduelle.
- Présence d'un espace suprachoroïdien (supraciliaire) hyporeflective.

Mesure des dimensions:

La mesure des dimensions de l'espace et l'épaisseur de la MTD intrascléral a été effectuée en utilisant l'étrier installé dans le système d'exploitation Aviso UBM **(figures 13.5 et 13.6).**

RÉSULTATS:

Vingt-huit patients (28 yeux) qui répondaient aux critères d'inclusion/exclusion ont été inclus dans l'étude. Les données démographiques et le diagnostic sont résumés dans le **tableau 14.1.** Toutes les 28 chirurgies ont été effectuées sans aucune complication peropératoire. Après l'opération, un seul cas (3.6%) a souffert d'hyphéma (2mm) au premier jour, et la résolution spontanée a eu lieu sans traitement. Au 80eme jour, dans un autre cas (3.6%), un détachement du corps ciliaire a été noté avec hypotonie sévère ultérieure. Le patient a été observé, sans aucun traitement spécifique, le rétablissement spontané du corps ciliaire a été spontanément obtenu. On ne signale pas de fuites (Seidel positif), les réactions inflammatoires à l'implant de collagène ou une incarcération de l'iris dans la MTD.

À 12 mois, la PIO préopératoire moyenne de 24.0 ± 5.8 mmHg a chuté à 11.7 ± 2.6 mmHg **(figure 14.1).** Par conséquent, à 12 mois, il y avait une réduction de la PIO de 51.4% (P <0.001) **(figure 14.2).** Les procédures d'appoint pour contrôler la PIO, comme le needling avec injection d'anti-métabolites ou goniopuncture ont été nécessaires dans 16 des 28 yeux. Parmi les16 yeux, 6 ont nécessités plus d'une procédure. Le nombre moyen de procédures nécessaires était de 2.43 (P <0.12). La PIO moyenne de ces 16 yeux avant de la première procédure était de 19.2 ± 3.41 mmHg. La durée moyenne postopératoire jusqu'à la première procédure d'appoint soit réalisée était de 84.9 ± 81.2 jours.

Le taux de succès complet à 12 mois est défini comme la proportion de patients présentant une PIO ≤21 mmHg sans l'utilisation de médicaments pour le glaucome avec ou sans goniopuncture ou needling. Le succès estimé est le même; il comprend également les patients qui ont besoin de médicaments hypotenseurs après l'intervention. À 12 mois, le taux de succès complet était de 86% et le taux de réussite était estimé de 96%, respectivement **(figure14.6).**

UBM analyse de la morphologie des bulles de filtration:

UBM une imagerie pour l'analyse de la bulle de filtration a été réalisée sur 9 des 15 yeux, sur une période de 12 mois. **Tableau 14.2** montre les caractéristiques démographiques des patients, les mesures de la PIO et la prise de médicaments anti-glaucomateux des 9 yeux qui ont été imagées.

La UBM a montré une bulle de filtration conjonctivale chez les 9 patients (100%), une l'espace intra-scléral chez 8 (89%), et supraciliaire (suprachoroïdien) avec une zone hypoéchogène dans 6 cas (67%). Le **tableau 14.3** présente la distribution de fréquence de chaque fonction UBM et les types de bulles de filtration conjonctivales détectées. Tout comme avec la UBM, une bulle de filtration conjonctivale était cliniquement visible à la lampe à fente dans l'ensemble des 9 yeux.

Six des neuf yeux avaient tous trois caractéristiques, deux yeux avaient deux caractéristiques et un seul œil eu juste une caractéristique. Dans le groupe avec 2 caractéristiques, une bulle sous-conjonctivale de filtration et un espace de décompression étaient présents; cependant, une zone hypoéchogène supraciliaire n'a pas pu être détectée. **Tableau 14.6** illustre la relation entre la répartition des caractéristiques UBM détectées en corrélation avec la réduction de la PIO, la prise de médicaments abaissement de la PIO et le volume de l'espace intra-scléral. Chez les 6 patients avec présence simultanée de tous les caractéristiques UBM, le taux de réussite dans l'atteinte de la PIO cible etait de 89%. Cet objectif n'a pas été atteint chez les patients avec 1 ou 2 caractéristiques. Par conséquent, les niveaux de PIO inférieurs ont été obtenus lorsque les 3 caractéristiques étaient présentes.

DISCUSSION:

Sclérectomie profonde (SP) avec l'implantation d'un dispositif de maintien dans l'espace suprachoroïdien est une technique relativement nouvelle, même si l'idée de réduire la PIO en dirigeant l'humeur aqueuse dans cet espace ne l'est pas. De multiples études ont été publiées concernant SP avec implants maintien de l'espace intra-scléral, cependant, un seul essai clinique (de Muñoz) a été publié dans le cadre de SP seul avec l'utilisation d'implants dans la région suprachoroïdienne. Muńoz a analysé l'efficacité du SP avec l'utilisation d'un implant T-flux, avec le corps du dispositif placé dans l'espace suprachoroïdien et les bras dans le canal de Schlemm. Il a rapporté un taux de succès complet (PIO <22mm Hg sans médicament) dans 73.8% de cas, et un taux de réussite estimée (PIO <21mm Hg avec ou sans médicament) à 93.4%, à 1 an.

Dans notre étude, le taux de succès complet à 12 mois était de 86%, le taux de réussite était estimé à 96%, avec une PIO moyenne de 11.7 ± 2.6 mmHg, des réductions générées de la PIO moyenne sont de 51.4%. L'utilisation préopératoire de médicaments anti-glaucomateux oculaires a diminué d'une moyenne de 2.57 ± 1.07 à 0.18 ± 0.39 à 12 mois après l'opération. Les résultats de la PIO à moyen terme et les taux de réussite chirurgicale dans cette étude sont similaires à ceux rapportés à ce jour pour SP réalisée avec un implant de collagène intrascléral, ainsi qu'à l'étude menée par Muñoz.

Comme dans d'autres études de sclérectomie profonde, qu'elle soit étudiée seule ou en comparaison avec la trabéculectomie, les complications postopératoires dans notre essai clinique étaient minimes. L'insertion de l'implant de collagène dans l'espace suprachoroïdien par les deux chirurgiens expérimentés qui ont exécuté la chirurgie a été décrite comme étant simple et directe, nécessitant moins d'effort et manœuvres que l'implantation dans l'espace intra-scléral. Aucune complication liée à l'insertion de l'implant de collagène dans l'espace suprachoroïdien n'a été signalée.

L'UBM peut être utilisée pour évaluer la morphologie et les changements du tissu résiduel après la chirurgie du glaucome. Elle fournit des informations qui ne peuvent pas être récupérées avec un examen à la lampe à fente. Elle permet la visualisation interne du site chirurgical et la mesure des dimensions de l'espace et l'épaisseur de MTD intra-sclérale. L'un des objectifs de cet essai clinique était d'analyser les voies d'écoulement de l'humeur aqueuse par l'étude de la corrélation du contrôle de la PIO avec la morphologie de quatre caractéristiques, trois d'entre elles sont des itinéraires de l'écoulement aqueux. Ces trois signes d'élimination aqueuses sont la bulle de filtration sous-conjonctivale, l'espace intra-scléral et de la zone hypoéchogène supraciliaire. La quatrième caractéristique morphologique examinée était la MTD.

Dans cette étude, seulement neuf des vingt-huit yeux inclus dans le procèssus ont subi une imagerie UBM pour l'analyse de la bulle morphologie et la facilité d'écoulement (31%). Même si cela est une petite fraction du nombre total d'yeux impliqués dans l'essai clinique, d'autres études ont inclus des chiffres similaires.

Dans notre étude, la détection d'un espace intra-scléral et d'une MTD était une conclusion commune. Le volume de l'espace intra-scléral ne semble pas être associé à un contrôle de la PIO (P = 0.02). D'autre part, l'épaisseur de la MTD n'a pas de corrélation avec la régulation de la PIO (P = 0.05). Une corrélation significative a également été observée entre l'écoulement aqueux suprachoroïdien et le contrôle de la PIO (P = 0.05). La présence ou l'absence d'une bulle de filtration sous-conjonctivale ne semble pas être associée à un contrôle de la PIO; comme estimé le succès chirurgical a été obtenu chez un patient sans une bulle de filtration, et dans l'autre avec une bulle encapsulée. La présence simultanée d'un espace intra-scléral, une bulle sous-conjonctivale et une zone hypoéchogène supraciliaire, a été associé un abaissement de la PIO et au taux de réussite chirurgicale.

En résumé, dans cette étude, le débit suprachoroïdien semble jouer un rôle dans la réduction à mi-parcours de la PIO; cependant, l'effet à long terme doit encore être évalué. La durée limitée de suivi (12 mois) et l'absence d'un groupe témoin dans cette étude présentent certainement des défis considérables. Il existe des rapports contradictoires concernant l'importance de l'espace suprachoroïdien dans CNPG et son rôle dans l'écoulement aqueux, donc de nombreuses questions doivent encore être étudiées. La possibilité de cette espace restant après de longues périodes doit encore être évaluée.

En conclusion, la SP avec implant de collagène suprachoroïdien semble être une méthode chirurgicale sans danger et efficace pour la réduction de la PIO.

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